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The incidence of inflammation among patients suffering from cervix cancer with positive beta haemolytic streptococci cultures from genital tract

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ABSTRACT

Aim: The main goal of this investigation was to evaluate the influence of positive beta haemolytic streptococci culture from the genital tract on patients receiving radiation therapy who suffer from cervical cancer. The other aim was to observe radiation therapy complications.

Background: Group B streptococci (GBS), group C streptococci (GCS) and group G streptococci (GGS) have been described as frequent invasive pathogens in elderly patients, often in association with underlying medical conditions including immunodeficiency and cancer.

Materials and methods: In the years 2006–2015, vaginal swabs from 452 patients were examined. A total of 118 women with positive beta haemolytic streptococci (BHS) groups A, B, C, F, G cultures were analysed, of whom 111 were diagnosed with cervix cancer of IB to IVA degree according to the FIGO 1988 clinical classification.

Results: Of the 452 patients suffering from cervix cancer 26.1% were positive for A, B, C, F or G group BHS isolated from the genital tract. All of the 114 examined strains were sensitive to beta-lactam antibiotics. The antimicrobials for which resistance was noted were erythromycin, clindamycin, ciprofloxacin and tetracycline.

Conclusions: Positive cultures of BHS from the genital tract were demonstrated to occur in patients with cervix cancer. Complications were found during radiotherapy in 30 (27%) of these patients, including 20 (18%) patients suffering from clinical symptoms of inflammation. When beta-lactam antibiotics are not recommended because of allergy, sensitivity tests to other drugs are necessary.

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1. Background

Lancefield group A streptococci (GAS) and group B streptococci are considered the major pathogenic beta-hemolytic streptococci (BHS) but other non-group A or B beta haemolytic streptococci that are frequently normal inhabitants of human body are also capable of causing significant disease.[1,2] Group B streptococci (GBS), group C streptococci (GCS) and group G streptococci (GGS) have been described as frequent invasive pathogens in elderly patients, often in association with underlying medical conditions, including immunodeficiency and cancer.[2,3] According to Ekelund et al., GBS dominated BHS infections because of peri- or post-operative procedures. Cancer was the second most frequent predisposing factor.[2]

2. Aim

The main goal of this investigation was to evaluate the influence of positive beta haemolytic streptococci culture from the genital tract on patients receiving radiation therapy who suffer from cervical cancer. The other aim was to observe radiation therapy complications.

3. Materials and methods

Microbiological examinations of the genital tract in patients suffering from cervix cancer were introduced as a standard method in the Department of Radiotherapy and Gynaecological Oncology at the Greater Poland Cancer Centre.

3.1. *Patient characteristics*

In the years 2006–2015, vaginal swabs from 452 patients were examined. A total of 118 women with positive beta haemolytic streptococci (BHS) groups A, B, C, F, G cultures were analysed, of whom 111 were diagnosed with cervix cancer of IB to IVA degree according to the FIGO 1988 clinical classification: one patient with IB degree, 25 patients with IIB degree, 76 with IIIB, 6 with IVA and 3 with IVB, while 7 patients were treated because of vaginal cancer and corpus uteri cancer with infiltration to cervix. In all cases, clinical findings were consistent with histopathological diagnosis.

The age of the patients was from 30 to 87 years, average 55.4.

The severity of complications was classified according to the CTC (Common Terminology Criteria for Adverse Events – version 4.0) classification with the exception of neutropenia which was estimated according to the Radiation Therapy Oncology Group (RTOG).

Among 111 patients with cervix cancer, 90 received radical radiotherapy which consisted of external beam radiotherapy combined with intracavitary brachytherapy.

Conformal radiotherapy was administered with 15 MV photons, using a conventional 4-field box technique (opposing anterior and posterior fields, and two opposing lateral fields).

Clinical treatment volume covered tumour of the vaginal fornix and walls, parametria and pelvic lymph nodes. Teletherapy was combined with high-dose brachytherapy (HDR) delivered with anatomy-adjusted applicators (tubes, ovoids, cylinders and needles). The methods of brachytherapy used were 2D and 3D MRI. The patients were given four fractions of treatment. In the group of radically treated women, 57 received concurrent chemotherapy (radiochemotherapy) – cisplatin 40 mg/m^2 given on a weekly basis (5–6 administrations), including patient of IB degree.

Due to advanced stage of cervix neoplastic disease, 21 patients (18.91%) were qualified for a shortened, palliative irradiation of the pelvis with the use of two AP–PA opposing beams technique to be given in one or two series. Three of them received BRT after two series of short therapy.

Table 1 – Sensitivity to erythromycin, clindamycin, ciprofloxacin and tetracycline of beta haemolytic streptococci isolated from vaginal swabs.

Drug name	Group of beta haemolytic streptococci				
	The number of sensitive strains (%)				
	A	B	C	F	G
Erythromycin	4(100)	52(81.3)	25(96.2)	4(100)	20(100)
Clindamycin	4(100)	54(84.4)	25(96.2)	4(100)	20(100)
Ciprofloxacin	3(75)	12(18.6)	2(7.7)	1(25)	2(10)
Tetracycline	2(50)	5(7.8)	14(53.9)	2(50)	8(40)

3.2. *Swab culture and sensitivity tests*

The vaginal swabs were cultured on the following microbiological media: blood agar, selective media for Gram-negative bacilli, chromagar for yeasts, coccosel agar, cetrimide agar, broth medium. Microorganisms were identified according to standard biochemical tests, which identified the most isolated strains to the genus level and many to the species level. The API 20 or Vitek 2 identification system (bioMérieux, Marcy l'Etoile, France) was used for confirmation. Beta haemolytic streptococci were identified on the basis of bacterial colony morphology on blood agar and Api Strep or ID GP system (bioMerieux). Group specific carbohydrates of streptococcal cell wall were used to classify the genus serologically according to the Lancefield system. Antibiotic sensitivity was assessed using the ATB and AST GP system (bioMerieux).

4. Results

Of the 452 patients suffering from cervix cancer, 26.1% were positive for A, B, C, F or G group BHS isolated from the genital tract. All of the 114 examined strains were sensitive to beta-lactam antibiotics. The antimicrobials for which resistance was noted are shown in Table 1: there were erythromycin, clindamycin, ciprofloxacin and tetracycline. In the years 2007–2010, there was no increase in BHS resistance to antibiotics used in the study. BHS strains were classified into 5 groups: A, B, C, F, G according to the Lancefield classification system – Table 1. The most frequently isolated BHS belonged to group B, C and G, 64, 26 and 20 strains, respectively. Four BHS group A and four BHS group F were isolated, as well.

The woman classified in IB degree severity receiving radiochemotherapy, reported fever and cystitis with dysuria but without changes in the process of treatment.

Table 2 – Prevalence and severity of complications during radio/radiochemotherapy with exceptions of neutropenia patients.

Complications	Staging	Grade		
		I	II	III
Colitis	I B		1	1
	III B		1	
Subileus	II B		1	
	III B			3
Cystitis	I B		1	
	II B		1	1
	III B		8	
Diarrhoea	II B	2		1
	III B		1	2
PID	II B		1	
	III B		4	1

Staging of cervical cancer according to FIGO 2009. Grading of adverse events according to NCI CTCAE v 4.03.

Complications and interruptions during radiation therapy were observed in 30 (27%) of 111 patients with positive BHS vaginal culture – Table 2.

In the group of patients with degree II B, colitis was observed in two women (1 in grade II and 1 in grade III) and diarrhoea in three women (2 with grade I, 1 with grade III), one grade II patient developed subileus. Cystitis with dysuria was only found in two cases (1 in grade II and 1 in grade III). In one degree II B patient, we noticed PID with fever. In all situations, interruption of radiotherapy was involved. Among women from the IIIB group, the most frequent complications were cystitis observed in 8 women (all in grade II) but only in four patients the process of radiotherapy was changed. Five patients from this group had diagnosed PID (4 in grade II and 1 in grade III) with fever and symptoms of peritonitis and with interruption in radiotherapy. Three patients with diarrhoea (1 in grade II and 2 in grade III) one with colitis (grade II) and three with symptoms of subileus (grade III) were the next group with complications during radiotherapy. The interruption of therapy in all situations was required, but in two cases dose reduction to 34.2 Gy/19 fr was necessary, as well. None of the 21 patients who had received palliative radiotherapy showed interruption in this treatment.

During radio/radiochemotherapy, we observed neutropenia which occurred with the other complications. The IIB degree patients showed neutropenia during radiochemotherapy in 3 cases (all grade III), but those with degree IIIB in 10 cases (8 grade II, 2 grade III). Neutropenia as an isolated complication was noticed in 2 women and in both of them the application of filgrastim was needed. During radiotherapy, this problem occurred in two patients (both grade III) and in one case the reduction of PTV was necessary.

The intervals in radiotherapy among patients who underwent radiochemotherapy were from 3 to 8 days (on average 5 days), except from the intervals due to neutropenia which were from 10 to 17 days (on average 13.6 days). Women treated only by radiotherapy had the intervals of 3–7 days (on average 5.3 days).

The patients from the group with complications during radiochemotherapy with degree IIB received, on average, 4.62 doses of cisplatin (40 mg/m^2) versus 3.89 in degree IIIB. Patients without complications received 5 and 4.93 doses, respectively.

Among the women with complications during radio/radiochemotherapy, two showed positive cultures for GAS. One of them had PID (grade III) and the other one had cystitis (grade II).

5. Discussion

The results of the tests performed showed that the most frequent isolated BHS in patients suffering from cervix cancer was GBS – 54.2%, while most pathogenic GAS constituted 3.4% of isolated BHS. GBS, GCS and GGS, have been described as frequent invasive pathogens in patients often in association with underlying medical conditions including immunodeficiency and cancer,[3–7] or advanced age.[2,8–10]

The rate of invasive GBS disease in adults continues to rise.[3,7,9,11] The incidence of invasive GBS among nonpregnant adults has increased twofold to fourfold over the last 2 decades.[9]

On the other hand, there are limited publication data concerning cultures of BHS from patients with cervix cancer.[12] One of our patients who had received radiochemotherapy showed positive vaginal culture for GAS. This patient developed PID. No information was found in the available literature about PID caused by GAS in patients suffering from cervix cancer.

Despite more than seventy years of the use of beta-lactams antibiotics, no resistance against these drugs among BHS has been reported. All isolated BHS strains demonstrated sensitivity to beta-lactams included in ATB Strep tests and to vancomycin and teicoplanin. All examined GAS, GCS, GFS and GGS were sensitive to erythromycin and clindamycin. 18.7% of GBS strains were resistant to erythromycin and 15.6% were resistant to clindamycin, while 3.8% GCS were resistant to these two antibiotics. Only 7.7% of GCS and 7.8% of GBS strains displayed sensitivity to ciprofloxacin and tetracycline, respectively (Table 1). Other authors have also described the sensitivity to penicillin and cephalosporin of groups A, B, C, F, G streptococci.[1,13,14] The antimicrobials for which resistance was noted were macrolides, clindamycin, fluoroquiunolones and tetracycline.[1,14–16] The resistance of BHS to these antibiotics seems to be highly variable between countries and increased over the years.[1,2,13,17] Some infections caused by BHS can be asymptomatic, but their identification may be crucial, especially in immunocompromised patients, to prevent further morbidity and mortality. Additionally, the absence of clinical symptoms of an ongoing acute inflammation in the genital tract does not rule out the possibility of such etiological agents causing inflammation in small populations.[18] Confirmed radiotherapy of our patients was administered with 15 MV photons. According to Tyagi et al., intensity modulated radiotherapy (IMRT) generated by 15 MV photon energies was used for treatment of cervix cancer, as well.[19]

Pelvic organs morbidity after irradiation of cancer patients remains a major problem, although new technologies have been developed and implemented.[20] On the other hand, the

quality of the brachytherapy planning methods helped in decreasing treatment toxicity.[21,22]

6. Conclusion

Positive cultures of BHS from the genital tract were demonstrated to occur in patients with cervix cancer. Complications were found during radiotherapy in 30 (27%) of these patients, including 20 (18%) patients suffering from clinical symptoms of inflammation. When beta-lactam antibiotics are not recommended because of allergy, sensitivity test to other drugs is necessary.

Conflict of interest

None declared.

Financial disclosure

None declared.

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