

# GLASSY CELLS ADENOCARCINOMA OF THE UTERINE CERVIX IN YOUNG PATIENT WITH HPV: CASE REPORT

*ADENOCARCINOMA DE CÉLULAS GLASSY DE COLO DE ÚTERO EM PACIENTE JOVEM COM HPV: RELATO DE CASO*

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## ABSTRACT

**Introduction:** cervical cancer is the second most common cancer in women worldwide and the third among the female population in Brazil. HPV plays an important role in the development of cervical cancer, being present in 95% of cases of cancer of the cervix. Glassy cells carcinoma is a poorly differentiated mixed adenosquamous carcinoma, rare, aggressive and highly resistant to radiotherapy. It typically affects young women, with peak incidence between the third and fourth decades of life. It is associated with types 16 and 18 of HPV and its evolution is accelerated during pregnancy. The average survival time after diagnosis is 10 months. **Case report:** woman, 26 years old, multiparous, with a history of condyloma acuminata, genital lesions that had increased in their last pregnancy, having evolved with exophytic masses diagnosed as glassy cell carcinoma, and aggressive course with early metastases not responsive to radiation therapy and progression to death in 16 months. **Conclusion:** glassy cells carcinoma is distinguished by aggressiveness and speed of its development, leading child-bearing age and productive young women to death. In view of its low response to anticancer therapies, we highlight the importance of its prevention, early diagnosis and treatment, possible through the use of condoms, the vaccine against HPV and cervical cytology at regular collection of endocervical material and effective monitoring.

**Keywords:** cancer of the cervix, glassy cells, HPV, prevention, STD.

## RESUMO

**Introdução:** o câncer de colo uterino é a segunda neoplasia mais comum em mulheres no mundo e a terceira entre a população feminina brasileira. O HPV desempenha um importante papel no desenvolvimento de neoplasias cervicais, estando presente em 95% dos casos de câncer de colo de útero. O carcinoma de células *glassy* é um carcinoma adenoescamoso misto pouco diferenciado, raro, de comportamento agressivo e altamente resistente à radioterapia. Atinge tipicamente mulheres jovens, com pico de incidência entre a 3ª e a 4ª década de vida. Está associado aos tipos 16 e 18 de HPV e sua evolução é acelerada na gravidez. O tempo médio de sobrevida após o diagnóstico é de 10 meses. **Relato de caso:** mulher, 26 anos, multipara, com história prévia de condiloma acuminado, apresentou lesões genitais que agravaram em sua última gestação, tendo evoluído com massas exofíticas diagnosticadas como carcinoma de células *glassy*, com curso agressivo e metástases precoces, não responsivo à radioterapia e progressão ao óbito em 16 meses. **Conclusão:** o carcinoma de células *glassy* destaca-se pela agressividade e rapidez de seu desenvolvimento, levando ao óbito mulheres jovens, em idade fértil e produtiva. Diante da sua baixa resposta às terapias antineoplásicas, destaca-se a importância de sua prevenção, seu diagnóstico e tratamento precoces, possíveis mediante o uso de preservativos, da vacina contra o HPV e do exame colpocitológico regular, com coleta de material endocervical e acompanhamento eficaz.

**Palavras-chave:** câncer de colo de útero, células *glassy*, HPV, preventivo, DST

## INTRODUCTION

The cervical cancer is the second most common cancer in women worldwide (15% of all cases). In Brazil, cervical cancer is the third most common in the female population, overcome by non-melanoma skin cancer and breast cancer. Consists of the fourth cause of death for cancer<sup>1</sup>.

HPV infection is present in more than 90% of cervical cancers and represents the main risk factor for developing cervical cancer, which is why its carcinogenic role has been highlighted as special study<sup>2</sup>. Despite this prevalence, only a small fraction (between 30-10%) of women infected with a type of high risk carcinogenic HPV will develop cervical cancer<sup>1</sup>. The most susceptible population to HPV infection comprises the age group from 18 to 28 years, and their main route of transmission is sexual.

A recent study showed that the risk of developing cervical cancer in women with HPV infection is 19 times larger. Women with oncogenic types 18, 31 or 33 have a risk 50 times higher, com-

ring to those not infected. If we consider the HPV 16, that risk rises to more than 100 times<sup>2</sup>. The persistence of infection is associated with increased risk of developing cervical intraepithelial neoplasia, especially when types 16 and 18 are present<sup>3</sup>.

Glassy cells carcinoma was originally described in the uterine cervix by Glucksmann and Cherry, in 1956. Among all cervical carcinomas studied, it corresponds to only 1-5%. It is a poorly differentiated adenosquamous carcinoma, rare, accounting for less than 1% of invasive carcinomas. Some authors have questioned whether the glassy cells carcinoma is a true clinicopathological entity, favoring the interpretation that it represents a non specific solid growth pattern of poorly differentiated adenocarcinoma<sup>4</sup>.

It typically affects young women, with peak incidence between the third and fourth decades of life. This has already been detected in the endometrium, the fallopian tubes, colon and cervix, which is the site of greatest prevalence<sup>5</sup>. It is characterized by rapid growth of exophytic masses, aggressive and refractory to radiotherapy. There is a relation to infection by types 16 and 18 HPV, which already had their DNA detected in tumor cells of squamous glassy cells<sup>2</sup>. It is also associated with both the multiparity and the offense during the gestational period<sup>6</sup>.

On microscopic examination, one can observe the glassy cells, which exhibit increased size, abundant presence with eosinophilic cytoplasm in frosted glass or fine granular pattern, with prominent edges, enlarged nuclei with conspicuous nucleoli, high mitotic ac-

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tivity and usually an inflammatory infiltrate stroma predominantly composed of eosinophils and plasmatic cells<sup>4</sup>. Such cytoplasmic characteristics inspired such name as *glassy*, due to the vitreous aspect of the cell. To be so classified, glassy cells should occupy at least a third of the tumor<sup>7</sup>.

The prognosis is reserved due to the aggressive clinical course, the tendency to early invasion and nodal metastases. Patients with small exophytic masses tend to be diagnosed early and treated aggressively when they exhibit a better prognosis than patients with endophytic tumors. Aggressive treatment consists of radical hysterectomy and adjuvant irradiation<sup>7</sup>, even though it is not very responsive to radiotherapy.

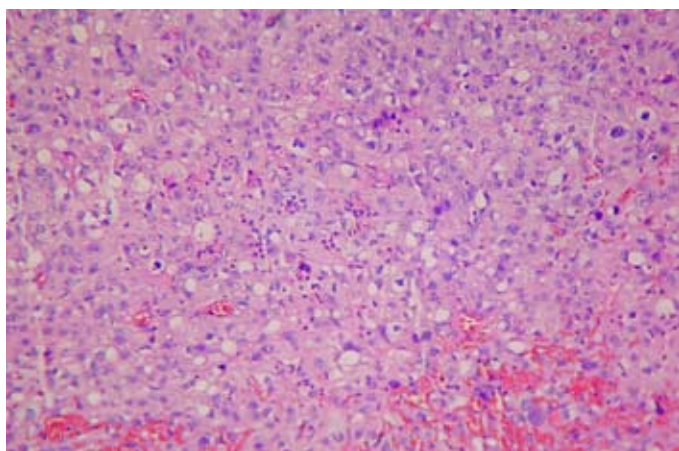
## CASE REPORT

Woman, aged 26, married, attended elementary school, housewife, born in the state of Bahia, residing in São Gonçalo – Rio de Janeiro, since 2005. Obstetric history of three pregnancies with outcome of normal delivery and no abortion. The last pregnancy occurred in 2005 and was marked by bleeding and threatened abortion.

Patient reported NIC I diagnosis and HPVcondylomatosis in 2004, in the state of Bahia, when she underwent cauterization of the uterine cervix for three months and follow up with implementation of preventive gynaecological examination every six months up to 2005. In the subsequent period, remained unattended because of her residences change and her last pregnancy. (SIC)

In 2007, she was admitted at the Hospital Universitário Antônio Pedro - UFF with hypogastric pain, bleeding, and fetid-smelling vaginal discharge, with four months of evolution. By colposcopic examination, a vegetative lesion on the cervix was observed, and histological analysis revealed to be a poorly differentiated carcinoma of the cervix, compatible with glassy cells carcinoma. She was treated with radiotherapy, chemotherapy, and intracavitary brachytherapy, all in full dose.

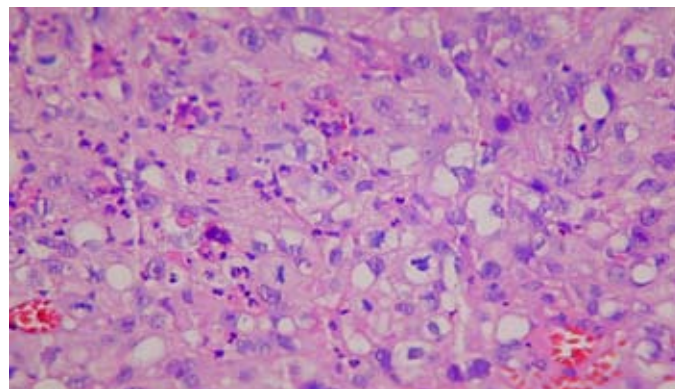
On 06/09/2008, sought emergency treatment complaining about abdominal pain. On that occasion an invasion of pelvic organs was identified, and the patient was referred to the palliative care unit for completion of the treatment protocol, taking into account the lack



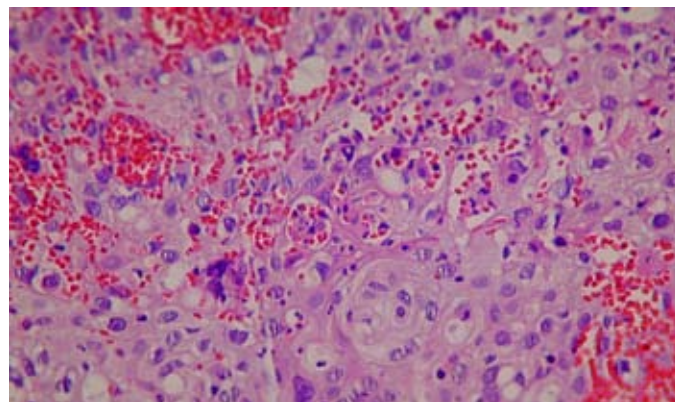
**Figure 1** – Epithelial neoplasia with polygonal cells, sometimes with clear vacuoles, intercepted by inflammatory infiltrate. There was no clear glandular formation, keratinization or intercellular bridges.

of response to any therapeutic measure. On 06/28/2008, returned to the emergency with pain in the right lower limb, and bone metastasis was diagnosed in right femur. Received analgesic therapy and was discharged on 06/30/2008.

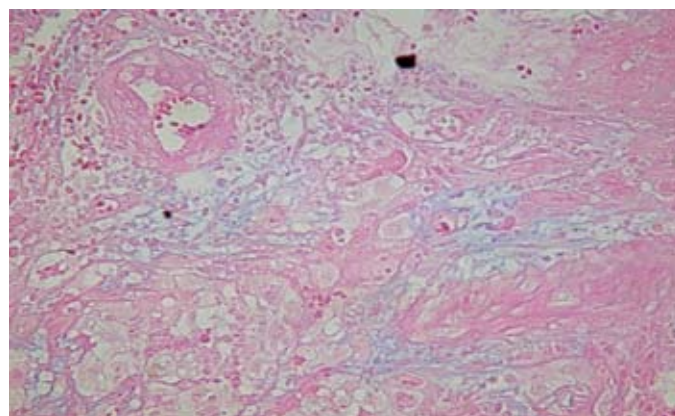
On 11/01/2008, returned to the Emergency with constant abnormal involuntary movements and profile consistent with acute renal failure, post-renal hydronephrosis, then being diagnosed with liver metastases. She was admitted to hemodialysis, opening picture of chickenpox after 15 days. On 12/04/2008, was discharged with recommendations for returning to dialysis three times a week.



**Figure 2** – Details of the inflammatory infiltrate with eosinophils, neutrophils and plasma cells.



**Figure 3** – Glassy cells carcinoma: cells with pleomorphism and discrete squamous aspect. Some cells exhibit enlarged nuclei, with prominent nucleoli and glandular cytoplasm.



**Figure 4** – Staining with Alcian blue, pH 2.5, shows deposits of mucin, thus identifying discrete glandular appearance.

On 12/22/2008, the patient was admitted to HUAP with tonic-clonic seizures, evolving to death in three days, due to hyperkalemia caused by chronic obstructive renal pelvic tumor generated by the invasion.

## DISCUSSION

The clinical case described showed typical features and evolved very similar to that described in the literature. This similarity becomes even more prominent because it is a rare pathology, and does not allow often description<sup>8,9</sup>. However, there are some case reports that call attention both for their similarities as for their differences.

The article described by Johnston *et al.*<sup>8</sup> presented three cases that occurred at University Hospital, in Chicago, in young patients (average of 25.5 years). All exhibited vaginal bleeding as initial complaint and one of them presented symptoms associated with pregnancy. The treatment of choice for the three was radical hysterectomy associated with pelvic lymphadenectomy and adjuvant radiotherapy. Two of them, including the pregnant woman, progressed to death in less than 1 year, while the other evolved favorably, and showed no sign of disease during 18 months of outpatient follow-up.

Ferrandina *et al.*<sup>10</sup> described the case of a 30-year old woman whose chief complaint was also vaginal bleeding. Cervical biopsy showed malignant lesion, and the option was for conization surgery. The final diagnosis obtained by histopathology was glassy cell carcinoma. The patient refused to perform any further processing, however, remained without evidence of disease during 38 months of follow-up.

The findings of extrapelvic extension in six of 13 patients observed in the study by Littman *et al.*<sup>11</sup> were also described, in contrast to the frequency found in 15% of cervical squamous carcinomas. In the same article, it was also observed the prevalence of cancer in younger women, besides the low survival of these patients, with a survival rate of 31% in five years.

Reviewing the literature, we observed a disease pattern, which includes our case: a young woman in the third decade of life, multiparous, with possible worsening of clinical symptoms during the last pregnancy, vaginal bleeding as initial complaint, refractoriness to radiotherapy, aggressive course, early invasion of neighboring structures, early metastasis and rapid progression to death. However, the outcome of this disease is still uncertain, as some cases respond to treatment and thus exhibit a better prognosis. Despite the progress of cases, the proposed therapy always includes radical surgery and radiotherapy<sup>8-10</sup>.

Given the aggressiveness of this disease, the rapidity of its evolution and the age of highest incidence, the importance of preventive monitoring through regular Pap test is highlighted. According to Deshpande *et al.*<sup>9</sup>, despite the aggressive evolution of glassy cell carcinoma, its early diagnosis may help in treatment response and thus improve prognosis. It is possible that this disease, in its early stages, occurs in an asymptomatic way or manifest itself through non specific symptoms, such as vaginal discharge, pain and bleeding, which reinforces the need for regular examination and preventive care for their first signs. In more advanced stages, the invasion of nearby structures can cause back pain, sciatica and acute renal failure after kidney with hydronephrosis, hematuria and hematochezia<sup>12-14</sup>.

Given the malignant presentation of this disease, there is urgent need to accomplish their prevention and early diagnosis. Such measures can be achieved through the use of condoms, the HPV vaccine and the regular preventive follow-up through col-pocitologic examination with the collection of cervical material from the cervical canal.

## CONCLUSION

The glassy cells adenocarcinoma is a rare and poorly differentiated adenosquamous carcinoma. Corresponds to less than 1% carcinomas, typically affecting young women (between the third and fourth decades of life), with rapid and aggressive progression as it was shown in the case. The proper diagnosis, treatment and monitoring of initial HPV infections can minimize such adverse outcomes.

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