wjpmr, 2019,5(5), 32-35

SJIF Impact Factor: 4.639

WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.wjpmr.com

Review Article

ISSN 2455-3301

WJPMR

NEUROENDROCRINE TUMORS OF THE UTERINE CERVIX, A CASE REPORT AND LITERATURE REVIEW

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Article Received on 13/03/2019 **Article Revised on 03/04/2019** **Article Accepted on 24/04/2019**

ABSTRACT

Neuroendocrine carcinoma is a rare and aggressive malignant tumour, small Cell neuroendocrine tumours of the uterine cervix represent 2% of cervical cancer. Given their rarity and the lack of randomized trials, the diagnostic and therapeutic management of these tumors is difficult and essentially based on that of pulmonary neuroendocrine tumours. Like the latter, and despite multimodality regimens, their prognosis remains unfavorable.Through this case, we report our experience in the management of these particular tumours while comparing our data with those of the literature. Resumé: Le carcinome neuroendocrinien est une tumeur maligne rare et agressive. Les tumeurs neuroendocrines à petites cellules du col utérin représentent 2% des cancers du col utérin. Compte tenu de leur rareté et de l'absence d'essais randomisés, la gestion diagnostique et thérapeutique de ces tumeurs est difficile et repose essentiellement sur celle des tumeurs pulmonaires neuroendocrines. Comme ces derniers, et malgré les schémas thérapeutiques multimodaux, leur pronostic reste défavorable. À travers ce cas, nous rapportons notre expérience dans la gestion de ces tumeurs particulières tout en comparant nos données avec celles de la littérature.

KEYWORDS: Small cell neuroendocrine carcinoma, cervix, radiation therapy, chemotherapy.

INTRODUCTION

Described for the first time in 1957,[1] Small cell carcinoma is a type of cancer neuroendocrine that originates in the cells of the system neuroendocrine. It tends to be aggressive and is associated with a less encouraging prognosis, even if diagnosed at a early stage. At through this case we report our experience in the management of neuroendocrine carcinomas small cervical cells while comparing our data to those of literature.

OBSERVATION

We report a case of 42 years old patient, without particular pathological antecedents, history of the disease goes back to 6 months by the appearance of the metrorrhagia of medium abundance, without digestive or urinary signs.

The speculum examination reveals a large cervical hemorrhagic mass of the anterior and posterior lip of the cervix, about 4 cm long, with involvement of the upper 1/3 of the vagina. And on digital rectal examination we have a centro-pelvic mass with distal parametrial infiltration to the left.

Biopsy with anatomopathological study: slightly differentiated proliferation of carcinomatous appearance

Immunohistochemical study:
Anti cytokeratin antibody: 40%positive
Anti CD56 antibody: 80% positive
Anti synaptophysin antibody: 100%positive

The immunohistochemical aspect compatible with a neuro-endocrine carcinoma Pelvic abdominal CT scan: homogeneous thickening of the cervix of 23 mm, with small infiltration of the right parameter, without lymph nodes or hydronephrosis. (Figure 1).

Our patient was treated with concomitant radio-chemotherapy, at a dose of 46 Gy with a brachytherapy and a parametrial compliment of 10 Gy.

DISCUSSION

Neuroendocrine carcinoma is a rare and aggressive malignant tumor, mainly developing at the expense of the bronchial tree and digestive tract. It represents only 1 to 3% of cervical tumors which are predominantly squamous cell carcinomas.[2-4]

Its actual incidence is probably underestimated because it is described under different terminologies such as carcinoid tumor, argyrophilic cell carcinoma, apudoma, oat grain cell carcinoma, neuroendocrine carcinoma, atypical carcinoid, undifferentiated small cell carcinoma, or carcinoma. intermediate cells.[1,2,4]

In 1997 a classification in four sub types has been proposed by Albores-Saavedra et al.

The most frequent named neuroendocrine carcinomas with small cells, characterized by high mitotic activity, extensive necrosis, vascular invasion and which are frequently associated with human papillomaviruses. Other subtypes are large cell neuroendocrine carcinomas, differentiated neuroendocrine tumors, typical and atypical carcinoid tumors.[2]

These tumors occur at a median age of 42 years (20-87),[4,5] which seems younger than for squamous cell carcinoma of the cervix. Clinical symptomatology is nonspecific, and the most common signs are vaginal bleeding and leucorrhoea.

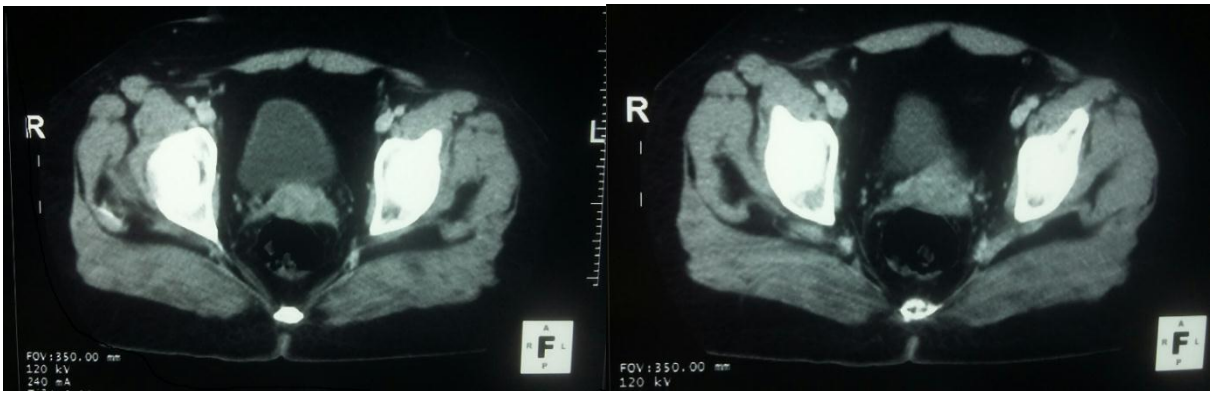

Figure 1: Ct scan showing cervical cancer of our patient.

As with squamous cell carcinoma of the cervix, these tumors are classified according to the classification of FIGO. They are often diagnosed later than squamous cell carcinoma of the cervix.[4] In contrast to the latter, which show their incidence and the number of evolved tumors at the time of diagnosis decrease thanks to the cervicovaginal smear, which is inefficient for detecting small-cell neuroendocrine carcinomas.[6,7]

This diagnosis is based on histological examination and more particularly on the immunohistochemical study.

Cervical biopsy often finds an undifferentiated type of tumor, and it is the presence of at least one neuroendocrine marker (synaptophysin, chromatogranin A, specific enolase neuron) that allows diagnosis.[8,9]

Because of the high propensity for regional dissemination and metastatic, the initial assessment should include abdominopelvic ct scan, preferably magnetic resonance imaging.[8]

Currently, and in order to improve ganglion staging PET (positron emission tomography showed superiority for pelvic and lumbar-aortic ; Allowing morphological and metabolic tracking of target lesions, and to better appreciate the effectiveness of a treatment.[10] AJM.

Staging follows that of all cervical tumors. However, it is important to recognize the increased risk of lymphatic invasion and the high rate of extra Pelvic recurrences. For example the early lymphatic invasion of Locoregional nodes were objectified in 40% of the stage IB small cell tumors less than 3 cm in diameter.

In 60% of these tumors the vascular and lymphatic invasion was found at the time of diagnosis.

The recurrence time is of 19.9 months.[8] Metastases are more commonly on the bone, and pulmonary.

Treatment of neuroendocrines cervical carcinomas is copied on that of the carcinoma squamous epidermis taking into account the characteristics of the neuroendocrine tumors of the lung.

For the localised tumours stage I-IIA, thetreatment local is not enough, two authorsbrought back disappointing results, Sheet et al., the first, found a rate of total survival at threeyears of 16% and one rate of survival without progresson at five years of 0%, For Sevin et al.,this last was of 36%,[11,12]

Relapses mainly hematogenous (67 to 90% of cases) and ganglionic (34% of cases), a high incidence of lymphadenopathies at diagnosis (40-60%), and frequent vascular invasion, are factors that prompted the majority of authors to associate a systemic treatment with local treatment,[13] Zivanovic et al. have compared retrospectively a local treatment alone (surgery) and a Local treatment associated with adjuvant chemotherapy.

They found a three-year recurrence-free survival rate of 83% for patients who received cisplatin and etoposide-based chemotherapy versus 0 % for local treatment alone. For advanced tumors, metastases are treated with combined platinum-based chemotherapy. While the initial response rate is quite high (50-79%) recurrence or chemoresistance develops. Then a 2 line therapy is started by vincristine / doxorubicin / cyclophosphamide and topotecan.

Because of the early metastatic spread rate, some authors preferred to use neoadjuvant chemotherapy, Chang demonstrated a complete response of 6 out of 7 patients

who received VAC (vincristine, adryamicine, and cyclophosphamide) / PE (cisplatine, etoposide) before hysterectomy; however, microscopic residues were present in all cases. Adjuvant chemotherapy was necessary. As a result, 3 patients were free at 16, 45 and 56 months of follow-up. Lee et al, on the other hand, did not show any benefit on the 6 patients who received neoadjuvant therapy.[14]

In the absence of trials comparing radiotherapy and surgery, some authors preferred to integrate them as part of a multimodal treatment. By combining surgery, radiotherapy and chemotherapy, Chan et al have achieved a five-year survival rate of 32%, which is significantly higher than those reported in the different series. Long-term survivors were those with size tumors less than 2 cm and undergoing radical surgery.[15] For locally advanced tumors (stages IIb-IV) and for inoperable patients, an association of radiotherapy and chemotherapy is recommended, according to the protocol of Hoskins et al.[16] At these stages, chemotherapy including at least five courses of cisplatin and etoposide are associated with a better probability of recidivism-free and specific survival.

In case of metastatic disease or recurrence, chemotherapy with either cisplatin or etoposide alone or alternating with VAC chemotherapy (vincristine, adriamycin and cyclophosphamide) is indicated. Prognostic factors are clinical stage, tumor size, presence and number of metastatic adenopathies, small cell histology and tobacco. The clinical stage was the only predictor of survival, 80% at stage I / II, and 38% at stage III / IV. The most common distant relapse sites are bone and lung (28%) rather than local relapse (13%).[17]

CONCLUSION

Neuroendocrine carcinomas with small cells of the cervix uterine are rare tumors, of unfavorable prognosis, but, thanks to the multimodal treatment, encouraging results have been shown in the latest series in case of early detected tumor, even if the best therapeutic scheme remains to be defined.

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