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Severe Hypercalcemia in Penile Squamous Cell Carcinoma: Case Report

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Abstract:- Hypercalcemia during cancer progression may reflect the expression of hypersecretion of PTH-related peptide (PTH-rp). This observation illustrates the possibility of malignant humoral hypercalcemia (MHH) in penile cancer in an 82-year-old patient treated at the Émile Durkheim Hospital in Épinal, France.

Keywords:- *Squamous Cell Carcinoma, Penile Cancer, Hypercalcemia, Humoral Hypercalcemia of Malignancy, Surgery, Urologic Oncology.*

I. INTRODUCTION

Penile cancer is the rarest cancer of the genitourinary system, especially in France [1]. The incidence is reported to be increasing. The rate in the world population may be 1 per 100,000.

Squamous cell carcinoma is the most common histological type (95%) [2].

At least one third of all squamous cell carcinomas are associated with HPV infection (most common strains HPV-16, HPV-6 and HPV-18) [3-4].

Several paraclinical tests have been proposed to follow the development and assess the extent of these tumours: Ultrasound, CT or MRI and, more recently, PET scanners.

Treatments for penile cancer are varied and always adapted to the TNM stage, the grade of the tumour. The prognosis remains poor: 80% survival at 5 years for N0 and 50% for N+ [4].

Circumcision in the neonatal period could reduce the risk of penile cancer but not PeIN [5]. However, adult circumcision is not preventive.

The CCAFU supports comprehensive vaccination for all young men (11–20 years) regardless of sexual orientation. This could protect men from HPV-induced cancers (penile, anal, oropharyngeal) but could also improve the protection of unvaccinated girls (cervical, anal, oropharyngeal) [4].

Humoral hypercalcemia of malignancy (HCM) is a rare but serious electrolyte disorder with a life-threatening prognosis due to its neurological, cardiac and renal complications. Whatever the cause, HCM requires urgent multidisciplinary management, first symptomatic and therapeutic, then diagnostic.

Squamous cell carcinoma of the penis is a tumor for which this abnormality has rarely been described. It is most commonly seen in the advanced stages of the disease in bone metastases.

Carcinomas (SCC) are collectively the most common cause of humoral hypercalcemia of malignancy, SCC of the penis rarely presents with hypercalcemia. Like in any other urologic malignancy, hypercalcemia in penile carcinoma tends to be associated with advanced disease and/or bony metastasis.

Hypercalcemia has also been reported without bony metastasis which is attributable to the paraneoplastic syndrome due to the expression of PTHrP [6]. Penile malignancy with hypercalcemia without bony metastasis was first reported by Anderson et al in 1965 [7]

The mainstay of treatment for cancer-related hypercalcaemia is hydration with normal saline and intravenous (IV) bisphosphonates [14-18].

Intravenous bisphosphonates should be given as soon as hypercalcaemia is diagnosed. They work by blocking osteoclast activity and subsequently reducing bone resorption.

Pamidronate and zoledronate are two commonly used intravenous bisphosphonates. In a trial comparing the 2 agents, zoledronate was found to be superior, particularly in achieving normal serum calcium levels faster, for longer and in more patients [19].

The dose of pamidronate is usually 90 mg in 500 ml of normal saline, infused intravenously over 2 to 4 hours. The dose of zoledronate is 4 mg intravenously over 15 minutes. It will be necessary to adjust the dose of bisphosphonates if there is renal impairment.

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II. CASE PRESENTATION

This is an 82 year old patient with oncological ATCDs TVNIM treated with RTUV plus BHCG, medical: diabetic, hypertension, ACFA and BPH, toxic: smoking cessation since 1984.

He was treated at the Émile Durkheim Hospital in Épinal, France, was diagnosed in May 2022 with squamous cell carcinoma of the penis, initially treated by total penectomy in May 2022 in anatomopathological: tumour of the glans measuring 3*2. 7 cm, corresponding to a moderately differentiated keratinising squamous cell carcinoma with an infiltrative nature involving the corpora cavernosa, no Vascular embolism, tumour extending to the level of the balano-preputial fold and the prepuce, total excision, stage pT1a.

In July 2022, bilateral lymph node development, beginning of August 2022: right inguinal dissection with anapath: N+ 4/7, capsular rupture for 3 lymphadenopathies.

The PET scan performed on 07/2022 showed a non-specific adenomegaly of the Barety compartment to be monitored.

A thoraco-abdomino-pelvic scan was performed on 09/08/2022, confirming the presence of bilateral external iliac adenomegaly and adenomegaly of the Barety compartment.

Clinically, patient with an OMS 1, no particular abnormalities, rhythm disturbances on auscultation, patient with a pacemaker, peripheral lymph node sites are clear.

PET scan performed on 18.10.2022: no pelvic development, persistence of adenomegaly of the barety compartment to be monitored.

Surveillance PET scan performed on 23.01.2023 showed a large confluent hypodense mass in the left inguinal fold with a fistulous course to the intensely hypermetabolic skin, with a rather infectious appearance. Absence of visceral or distant lymph node hypermetabolism, which may indicate continued tumour progression, with stability of the known lymph node in Brety's compartment.

Clinically: inguinal lymph node lesion fistulized to the skin with permeating nodules, inaccessible to surgical treatment or radiotherapy.

The file was presented at a multidisciplinary consultation meeting (RCP) at the Lorraine Cancer Institute in Nancy (CHU-ICL) on 26/01/2023 the decision was to carry out chemotherapy adapted to the age of the patient Carboplatin and Taxol weekly 3 weeks/4, if sensitivity or response included in the PULSE trial.

The patient was seen on 02/02/2024 in the presence of his family to discuss palliative chemotherapy for squamous cell carcinoma of the penis with continued progression of the inoperable left inguinal lymph node. The indication for chemotherapy with weekly CARBOPLATINE TAXOL was reiterated with the patient, whose general condition remains average.

Clinical examination confirmed a left inguinal mass which was fistulized to the skin and required daily care. There was no lymphoedema of the ipsilateral lower limb and no pain. On the day of the consultation, the patient was informed of the planned treatment, its side effects and risks. He had accepted the principle. We considered 2 months of treatment before an initial assessment of its efficacy. As mentioned in the RCP, if there is a partial response to treatment, we will discuss maintenance immunotherapy (PULSE trial).

We also informed the patient and his family about the seriousness of this pathology and the low chemosensitivity of the latter.

On 04/02/2023 the patient was then transferred to our department, his condition had actually deteriorated with marked asthenia and speech problems.

The clinical examination on admission confirms a serohematous and malodorous discharge at the level of the left inguinal region with a foul odour, and the presence of a 10 cm left inguinal mass with a 4 cm ulcero-necrotic lesion fistulized in its centre.

L'examen clinique d'entrée confirmera un écoulement séro-hématique et malodorant au niveau

Biological assessment revealed malignant hypercalcemia of 3.90 mmol/L in one patient who had no confirmed bone metastases on the most recent PET scan.

The hypothesis of malignant para-neoplastic hypercalcaemia has been raised. The PTH level is normal and the PTHrp level is very high value at 36,6 pg/mL (normal range < 13 pg/mL).

The patient had benefited from hyperhydration, then several infusions of SODIUM PAMIDRONATE, which unfortunately allowed a partial improvement of the hypercalcaemia, which quickly proved to be refractory.

In the oncological context, in the absence of an obvious therapeutic option and taking into account the patient's age, we maintained the indication for palliative care only.

The clinical situation deteriorated rapidly with the onset of altered consciousness on 11 February.

Death will occur without a satisfactory recovery of consciousness, in the presence of his family, on 13 February at the end of the morning.

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Table 1: Kinetics of Corrected Serum Calcium

Date	Corrected Calcium Value (Mmol/L)
04/02/2023	3.90
06/02/2023	3.46
07/02/2023	3.29
09/02/2023	3.15
11/02/2023	3.78

Table 2: List the Literature Available on Penile Cancer with Hypercalcemia

Author	No of Cases	Tumor Type	Bone Mestastases	PTHrp	Visceral Mets	Managements of Tumor	Outcome of Ypercalcemia
Dorfinger et al. [6]	1	SCC	A	E	P	Sugery, chemotherapy	Temporary
E. Anderson et al. [7]	1	SCC	A	U	A	Surgery	Resolved
Malakoff et al. [8]	1	Epidermoid carcinoma	A	U	P	Surgery, radiotherapy, bleomycin	Temporary
Trejo Rosales et al. [9]	1	SCC	A	E	A	Palliative	Controlled
Sardinas et al. [10]	1	SSC	A	N	P	Chemotherapy	Uncontrolled
Gandhi et al. [11]	1	SCC	A	U	P	Surgery, chemotherapy, radiotherapy	NA
R Kanta et al. [12]	1	SCC	A	E	A	Supportive	Temporary
CCK Ho [13]	1	SCC	P	U	A	Supportive	Resolved

Pthrp: Parathyroid Hormone-Related Peptide, SCC: Squamous Cell Carcinoma.
A: Absent, P: Present, U: Undocumented, N: Normal, NA: Not Available, E: Elevated.

- *Limit of the Study:* Our patient did not have a bone scan for the exclusion of bone metastases.

III. CONCLUSION

The occurrence of humoral hypercalcaemia of malignancy is rare in penile squamous cell carcinoma, it may or may not indicate recurrence or progressive continuation. Treatment is both symptomatic and specific. The prognosis is poor.

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