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Total neoadjuvant therapy for locally advanced rectal cancer in developing countries : about an observation in a private congolese clinic.

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Abstract

Locally advanced rectal cancer has benefited and continues to benefit from considerable advances in terms of therapeutic management. Total neoadjuvant therapy has shown benefit over radiotherapy alone or with concomitant chemotherapy in many respects. The case presented and discussed here is that of a Congolese patient diagnosed with locally advanced rectal adenocarcinoma managed by the OPRA regimen with induction chemotherapy who completed his neoadjuvant therapy alternately in his country of origin and abroad despite some toxic effects noted. The management of this case illustrates the possibility of allowing patients from developing countries to benefit from therapeutic advances in the management of cancer disease despite the significant challenges.

Keywords: locally advanced rectal cancer, total neoadjuvant therapy, OPRA

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Introduction

Locally advanced rectal cancer has seen a lot of progress in the last decade, in terms of therapeutic management. He is faced with a significant risk of metastasis and at the same time with difficulties in primary surgical sanction given the non-strictly localized nature; There is a possibility of making it curable. In the past, radiotherapy or radiochemotherapy was the modality par excellence to make the disease operable at this stage. It turned out that the resulting toxic effects, coupled with the lack of improvement in overall survival, were the main limitations.[12] From these shortcomings was born the idea of developing new approaches to improve adherence and compliance with treatment on the one hand, and to strengthen the effectiveness of neoadjuvant treatment on tumor volume on the other.[3] These new approaches, known as total neoadjuvant therapy (TNT), are characterized by the addition of full-dose neoadjuvant chemotherapy. Several strategies have been developed in this context, including OPRA with induction chemotherapy, OPRA with consolidation chemotherapy, RAPIDO, PRODIGE 23 essentially. It is clear here that at this stage of the disease, the 3 main treatment modalities in oncology find their place. To date, the DRC is not yet sufficiently equipped in terms of therapeutic infrastructure in oncology and one could imagine the difficulty of providing optimal and integrated care for patients with non-localized and non-metastatic rectal neoplasia in the country, yet the possibilities of cure are no longer to be proven. The case we report is an illustration of this difficulty which required shuttles between India and the DRC for care.

Medical observation

It was a 64-year-old Congolese patient who consulted a clinic in the city of Lubumbashi in the DRC for lower gastrointestinal bleeding for 6 months, transit disorders evolving for nearly 4 years and pelvic pain of more recent onset. On clinical examination, the general condition was good, performance status =1, the digital rectal examination found a mass whose exploration was completed by a lower gastrointestinal endoscopy and an abdominopelvic CT scan which revealed a circumferential rectal tumor infiltration in the form of an asymmetrical thickening predominant on the anterior side, stenosing and extending over 6.5cm in height. Its inferior pole was located 4 cm from the anal margin. He then consulted a medical training in India where an additional assessment was carried out:

CEA=288µg/L, PET-CT: hypermetabolism at the recto-sigmoid and proximal rectal level and at the level of the perirectal, pre-sacral and inferior mesenteric lymph nodes as shown in the appendix. There was no no signs of distant metastases. The diagnosis of high-risk high-risk locally advanced infiltrating Lieberkuhnian infiltrating adenocarcinoma was therefore made and treatment with neoadjuvant chemotherapy mFOLFOX6 followed by radiochemotherapy before performing a follow-up imaging assessment for possible surgery (robot-assisted anterior rectal resection) was prescribed.

The patient received 8 cycles of mFOLFOX6 from april 12th to july 23rd 2024 in the DRC, at the Ars clinic in Lubumbashi. This treatment was marked by a complete disappearance of pelvic pain and the occurrence of stage 4 neutropenia and grade 1 hand-foot syndrome, which were treated. Subsequently, he underwent a long chemoradiotherapy and a surgical treatment in India.

Discussion

The OPRA TNT regimens used induction or consolidation chemotherapy (before or after radiochemotherapy) based on a doublet (FOLFOX or CAPOX). Progression-free survival at 3 years, which was the primary outcome, was 78% and 77%, respectively. This regimen is one of those for which chemotherapy takes longer (4 months) compared to many other regimens (GCR-3: 3 months, PRODIGE-23: 3 months, CAO/ARO/AIO: 3 months), except compared to the RAPIDO regimen: 4.5 months, and exposure to the toxic effects of the molecules used can be understood.

Our patient had two episodes of severe neutropenia managed by supportive therapy, as well as hand-foot syndrome. This chemotherapy has been shown to be effective on the patient's symptoms. The stage of his disease and the male sex were similar characteristics to those of the patients included in the phase II OPRA trial. This leads us to believe that the patient had criteria that would not prevent the choice of this neoadjuvant strategy even if the topography of his tumor was far from the median reported during the trial. In this trial, 6.3% of subjects were black in the OPRA arm with induction chemotherapy while they represented 4.8% of patients in the cohort with consolidation chemotherapy.

It should also be noted that OPRA with consolidation chemotherapy had significantly better outcomes in terms of local recurrence post watch and wait and recurrence-free survival after total mesorectal resection, although the primary outcome (3-year progression-free survival) was similar in both cohorts. This is corroborated by the CAD/ARO/IOA trial, which instead evaluated the pathological complete response which was better in the arm with consolidation chemotherapy compared to the arm with induction chemotherapy, survival rates had not been evaluated[6] and the results of the former show many advantages of the OPRA strategy with consolidation chemotherapy over that with induction chemotherapy.

The patient would have liked to receive his entire treatment in Congo, but as material and human resources were lacking in the field of radiotherapy, this was not possible, the least expensive option was to receive chemotherapy at a relatively lower cost in one's country of origin and other treatment modalities outside the country.

From a diagnostic point of view, let us mention the valuable contribution of foreign hospital training in the refined evaluation of the extent of the tumor and its stage of evolution and its anatomopathological and molecular characteristics.

It should be noted here that there is an interest in receiving TNT rather than looking for other strategies that would be more available in developing countries (possibility of surgical intervention, possibility of having drug treatments,...).

This reflection highlights the need to improve the conditions of care for these patients, including those with locally advanced rectal cancer in our environments because the survival benefit is no longer to be proven in terms of TNT.

This patient makes several shuttles at his own expense, as his country of origin has only one radiotherapy center without necessarily having permanent trained chemotherapists.

Conclusion

This case illustrates the possibilities, albeit limited, of diagnosing and managing locally advanced rectal cancer in our setting. Patients in developing countries, including DR Congo, can also benefit from advances in the treatment of cancer diseases. But until now, this profit has been partly dependent on foreign countries. Our governments should equip our hospital training courses more.

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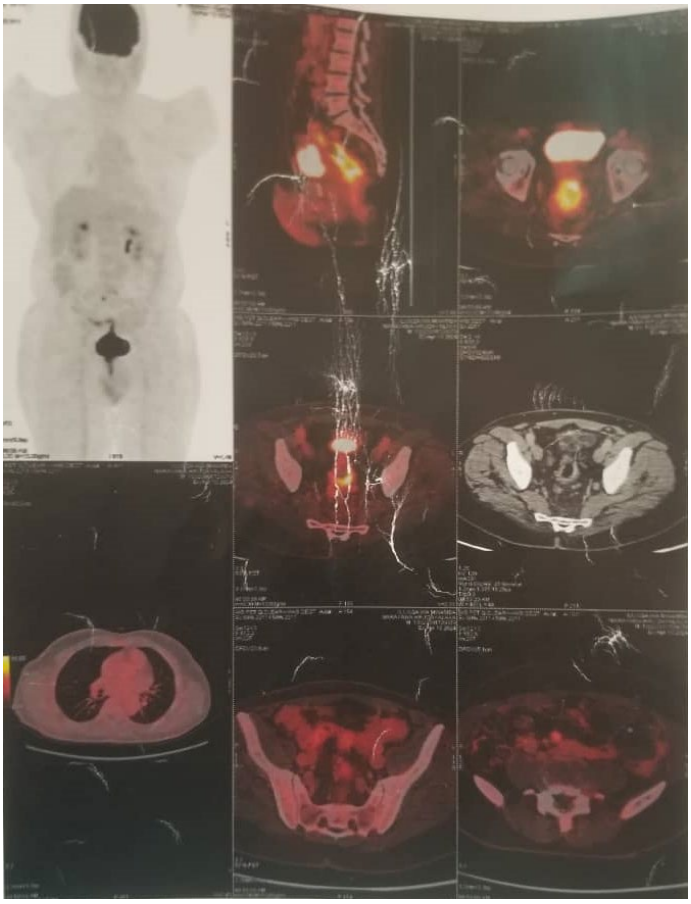
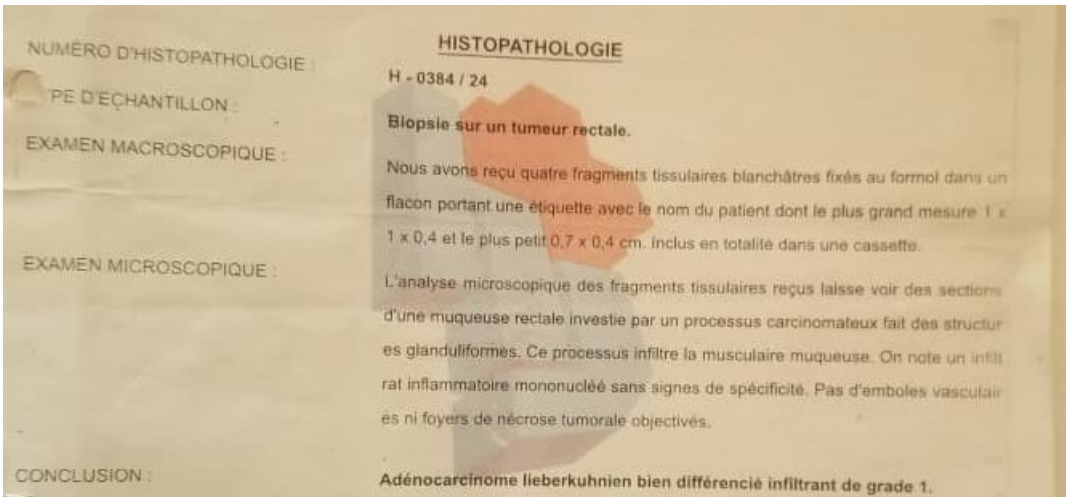
Appendix

1. PET CT images before treatment begins



2. Anatomopathologicals findings on the core biopsie of the rectal mass



NUMÉRO D'HISTOPATHOLOGIE :

PE D'ÉCHANTILLON :

EXAMEN MACROSCOPIQUE :

EXAMEN MICROSCOPIQUE :

CONCLUSION :

HISTOPATHOLOGIE

H - 0384 / 24

Biopsie sur un tumeur rectale.

Nous avons reçu quatre fragments tissulaires blanchâtres fixés au formol dans un flacon portant une étiquette avec le nom du patient dont le plus grand mesure 1 x 1 x 0,4 et le plus petit 0,7 x 0,4 cm. Inclus en totalité dans une cassette.

L'analyse microscopique des fragments tissulaires reçus laisse voir des sections d'une muqueuse rectale investie par un processus carcinomateux fait des structures glanduliformes. Ce processus infiltre la musculaire muqueuse. On note un infiltrat inflammatoire mononucléé sans signes de spécificité. Pas d'emboles vasculaires ni foyers de nécrose tumorale objectivés.

Adénocarcinome lieberkuhnien bien différencié infiltrant de grade 1.