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CASE REPORT **OPEN ACCESS**

Evidence that the use of progesterone receptor modulators/antagonists can provide palliative benefits for a moribund patient with cholangiocarcinoma

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A B S T R A C T

There is considerable evidence that most (if not all) malignant tumors utilize immunomodulatory proteins that result from activating membrane progesterone receptors (mPRs) in males as well as females. Support for this concept has been provided by the demonstration that treating people with a variety of different cancers that are very advanced with no more standard or even clinical trial options to have a considerable extension of life (in several instances even more than 5 years with death unrelated to their cancer) by treatment with single agent oral mifepristone a PR receptor antagonist. Just as important, most patients, even when the cancer has damaged vital organs, so a marked extension of life is not possible, are able to experience considerable palliative benefits. Presented is a case of an 85-year-old male whose end stage cardiomyopathy was complicated by a 5.5 cm cholangiocarcinoma with lymph node metastasis. Rather than the suggestion of hospice to end life within 2-3 weeks, or starting chemotherapy, he chose the option of mifepristone therapy. So far, he has experienced 4 months of a decent quality of life. The purpose of presenting his case is not only to introduce another type of cancer that responds to PR antagonists that has never been reported before, but to introduce this type of therapy for advanced cancer that despite many publications and presentations at scientific meetings, probably because there are no commercial interests, this highly effective therapy is relatively unknown, it may be especially of interest to countries, e.g., India and China, where mifepristone is available at a much lower price than in many other countries. The cost of healthcare could be markedly reduced by simply offering oral mifepristone to patients with advanced cancer and no need to monitor subsequent potential adverse effects because it has a very high safety profile when used at a lower dosage of 200mg/day. Thus, besides just a fraction of the cost of chemotherapy agents or immunotherapy, there would be considerable savings for cost of hospital admissions to treat the complication of most standard cancer therapeutic options.

Key Words: cholangiocarcinoma, membrane progesterone receptor, progesterone induced blocking factor, progesterone receptor antagonists, mifepristone, advanced cancers.

INTRODUCTION

There is evidence that activation of membrane progesterone receptors (mPRs) by rapidly growing cells e.g., the fetal placental unit and malignant tumors, results in the production of the immunomodulatory protein called the progesterone induced blocking factor (PIBF). This protein may allow both the fetus and the malignant tumor to rapidly proliferate, invade normal tissue, and evade immune surveillance (1-3). Treating patients with very advanced cancers of various types with the progesterone receptor (PR) modulator mifepristone has allowed not only considerable palliative benefits, but marked extension of life (4,5).

Progesterone receptor modulators are better for cancers that are devoid of the classic nuclear PR (nPR) or cancers initially positive for the nPR that becomes more aggressive when the tumor loses the nPR (6).

Most of the cancers where single agent mifepristone has been used for treatment have been stage IV with no more treatment options available. In the United States, related to the sensitivity of mifepristone used for therapeutic

abortion, there had been a requirement that the off-label use of mifepristone for treating cancer must receive a compassionate use investigation new drug (IND) application from the Food and Drug Administration (FDA). Nevertheless, clear considerable improvement of quality and frequent length of life has been reported in a large variety of advanced cancers (2-5). These include: 1-ademcarcinoma of the colon; 2-thymic epithelial cell cancer; 3-transitional cell carcinoma of the renal pelvis; 4- pancreatic cancer; 5-malignant fibrous histiocytoma; 6- glioblastoma multiforme stage IV; 7-leiomyosarcoma; 8-non-small cell lung cancer (NSCLC); 9 small cell lung cancer (SCLC); 10- breast cancer; 11-urothelial cancer (7,8). The only case approved for the use of mifepristone that was not very advanced was a middle-aged man with bilateral renal cell carcinoma. He is still alive and doing well, more than 25 years from initial therapy with single agent mifepristone despite no surgery for 3 lesions in his left kidney to prevent bilateral nephrectomy and the need for dialysis (9).

Reported here is the first case of demonstrating significant palliative benefits following treatment with mifepristone for an unrespectable cholangiocarcinoma in a moribund 85-year-old man dying of end stage congestive heart failure and non-malignant plural effusions related to a severe cardiomyopathy.

CASE REPORT

An 85-year-old man with a known history of cardiomyopathy was admitted to the hospital because of marked dyspnea on exertion related to large pleural effusions and pericardial infusion. Besides left sided heart failure he also had right sided heart failure causing edema of the lower extremities.

The large pleural effusions were drained and cytologic evaluation and cultures were performed. There were no cancer cells and cultures were negative. However, magnetic resonance imaging with or without gadolinium found a 5.5cm abdominal mass with local lymph node metastasis. Pathological examination found it to be a moderately differentiated cholangiocarcinoma.

The one recommendation from his physician team of cardiologists and oncologists was, based on his age of 85, cardiomyopathy and advanced heart failure, and a cancer known to be a very aggressive type, to consider hospice. Another recommendation was to insert a pleura-evac drainage system and start chemotherapy.

His daughter-in-law, who is a nurse in our practice and who knew of the signification extension of a high quality of life with single agent oral mifepristone and the general lack of side effects, advised him to insert the plural effusion drainage system, but instead of chemotherapy (and its many side effects), to initiate treatment with 200mg /day oral mifepristone.

This 85-year-old man still wanted to live, and he chose the mifepristone option. He chose not to have his cancer monitored for growth and metastases but merely take the daily pill and enjoy as much time as he could at home. So far, he has no symptoms from his cancer for 4 months, and the pulmonary drainage system is working well enough to afford him so far, an extension of life with relatively good quality but no symptoms related to cholangiocarcinoma or from mifepristone therapy.

DISCUSSION

Despite starting mifepristone when not only has the cancer greatly advanced, but generally after failures with various anti-cancer regimens, some patients are not only provided palliative benefits but live past 5 years (10-14). In fact, in many of these cases the death was not from the cancer progression but some comorbidity e.g. myocardial infarction or pneumonia (10-13). Most of the time significant extension of life and marked improvement of quality occurs despite the continued presence of some of the malignant lesions. Patients are warned that stopping the drug may lead to rapid progression of the cancer. Nevertheless, one man who was still alive 5 years later was convinced by his oncologist to try a new investigational drug and if it was not working, he could go back on mifepristone. The cancer spread so fast that he died before he could resume the mifepristone (7,14).

Sometimes cancer has created so much damage to various organs and blood vessels that a long extension of life may not be possible. Nevertheless, almost all patients report marked symptom relief even before regression of metastatic lesions are not noted as yet. Improved quality of life is also related to the lack of side effects of mifepristone vs significant side effects from most chemotherapy agents and even immunotherapy.

Thus, we think that this patient has made a wise choice; he so far has had 4 good quality months of life since the diagnosis, and hopefully we will also report significant life extension. There is a good chance he will die of end stage heart failure rather than his cancer.

In India, mifepristone is available at a very low price. The cost of healthcare is rising rapidly, and a significant proportion is related to expensive oncology drugs, and the cost of testing to evaluate the efficacy of treatment.

This man opted to have no more monitoring. Since generally there are no more treatment options once the lesions are widely metastasized, cost of health care could be markedly reduced by offering patients oral mifepristone with no more monitoring followed by palliative care options if the drug is no longer showing efficacy.

This is the first case of treating cholangiocarcinoma with mifepristone providing palliative benefits. Hopefully, if this 85-year-old man's heart can hold out, we hope to write a follow-up of single agent mifepristone providing increased longevity plus palliative benefits for cholangiocarcinoma.

Conflicts of Interest: None

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