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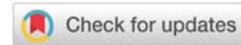
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Research Article

Selecting patients for treatment with immunotherapy: Our experience in a resource-deprived economy

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Abstract

Background: Majority of the solid cancer patients seen in our Centers come with advanced diseases. Some of the cancers are locally advanced, while others are metastatic. Most of these patients who present late belong to the poverty-stricken group in our community. Only few of them can afford costly drugs for their treatment. The government Health Insurance Scheme does not cover cancer patients in Nigeria.

Aim: To highlight the importance of immunotherapy in the management of metastatic cancers.

Objective: We wish to share our experience in the use of immunotherapy (Bevacizumab) for metastatic cancers in the few patients who could afford the drug, and to highlight the need for reduction of the prices of immunotherapeutic drugs, or for government to subsidize the costs.

Methods: From the 1,135 solid cancer patients treated in our two Centers in three years (February 2017 to January 2020), those who presented with metastasis were slated for immunotherapy after we had obtained their immunohistochemistry results.

Results: Six hundred and one (601) patients (53.0%) presented late. Three hundred and five (305) of these late presenters (50.7%) came with metastasis. Only 67 (22.0%) out of the 305 metastatic patients could afford immunotherapy, because of high cost. With the exception of one female patient, each of the remaining 66 patients was able to afford only one single dose of Bevacizumab (Avastin)[®]. Of these patients, one died of Tumor Lysis Syndrome following one single dose of 600 mg of Bevacizumab. There were measurable shrinkages of the tumor burdens, as well as improvement in the quality of life of the remaining 66 patients.

Conclusion: Following these encouraging results, immunotherapy for metastatic carcinomas is to be encouraged for wider use, even in resource-deprived economies. Repeated doses will offer the patient greater benefits. Government should subsidize the cost of immunotherapeutic drugs so that they would become affordable by majority of those who need them.



Introduction

Cancer has remained a worldwide scourge, refusing to respect international boundaries or racial differences. The outcome of cancer treatment depends largely on the time of presentation by the patient.

Late presentation has remained the problem with the management of cancers. This situation is more common in developing countries, compared to patients in advanced countries who present early for treatment. The reasons for this late presentation include the following: Fear, Denial, Poverty and Misinformation. Fear of cancer is heightened by the fact that some people have erroneously equated cancer to sure death. Because of ignorance, coupled with fear, some patients find solace in outright denial of the disease, in spite of a clear histological diagnosis. In this frame of mind, such patients would want to agree with quacks and charlatans who would tell them what they want to hear. In the background of poverty, these quacks and charlatans convince the patients to accept their cheaper treatment. When the disease worsens, and when it becomes obvious to the patients that the so-called Alternative Medicine is not helping them, the patients present to the surgeon with metastatic disease. This is where the use of immunotherapy becomes most helpful [1-4].

MicroRNAs (miRNAs) are known to regulate the expression of various oncogenes or tumor suppressor genes. The expression profiling of miRNAs has already entered into cancer clinics as Diagnostic and Prognostic biomarkers, to assess tumor initiation, progression, and response to treatment in cancer patients [5]. While tumor cells proliferate rapidly, they stimulate angiogenesis to provide oxygen and nutrient support after reaching a certain volume. Vascular endothelial growth factor (VEGF) signaling is an important target for cancer therapy because of its role in tumor angiogenesis, and its potential role in tumor cell survival and invasion. Bevacizumab acts as a monoclonal antibody against VEGF and can inhibit the formation of new vessels and tumor growth [6].

Immunotherapy has proved to be of great advantage in the treatment of metastatic breast carcinoma, especially when combined with chemotherapy [7-10], as well as in the treatment of metastatic colorectal carcinoma and hepatocellular carcinoma [10].

Patients and methods

A total of 1,135 solid cancer patients were treated in our two Centers (Nnamdi Azikiwe University Teaching Hospital, Nnewi and Gabro Specialist Hospital, Nnewi) in three years (February 2017 to January 2020). Those who presented with metastasis of breast cancer, colorectal cancer, or hepatocellular carcinoma were slated for immunotherapy after we had obtained their immunohistochemistry results.

Results

Six hundred and one (601) patients (53.0%) presented late. There were 225 males (37.4%) and 376 females (62.6%),

giving a M:F Ratio of 0.6:1. Their ages ranged between 32 years and 87 years (Table 1). Two males presented with breast cancer while 261 females presented with breast cancer. For colorectal cancer, there were 205 males and 112 females. For hepatocellular carcinoma, there were 18 males and three (3) women (Table 2). Three hundred and five (305) of these late presenters (50.7%) came with metastasis. Only 67 (22.0%) out of these 305 metastatic patients could afford immunotherapy, because of high cost. During this study period, the cost of 600 mg of Bevacizumab (Avastin)[®], to be given every three weeks, was one thousand and eighty-seven (1,087) US Dollars. The average family monthly income at the same time of study was thirty (30) US Dollars. With the exception of one female patient, a Nun, each of the remaining 66 patients was able to afford only one single dose of Bevacizumab (Avastin)[®]. Of these patients, an elderly male with carcinoma of the caecum, died of Tumor Lysis Syndrome following one single dose of 600 mg of Bevacizumab. Two (2) male patients presented with carcinoma of the breast.

Table 1: Age range and sex distribution.

| Age Range | Male | Female | Percentage |
|-----------|------|--------|------------|
| 30-39 | 1 | 12 | 2.2 |
| 40-49 | 3 | 35 | 6.3 |
| 50-59 | 7 | 101 | 18 |
| 60-69 | 55 | 164 | 36.4 |
| 70-79 | 101 | 63 | 27.3 |
| 80-89 | 58 | 1 | 9.8 |
| Total | 225 | 376 | 100 |

Table 2: Types of tumors and sex distribution.

| Type of tumor | Males(n) | Females(n) |
|-----------------------------|----------|------------|
| 1. Breast cancer | 2 | 261 |
| 2. Colorectal cancer | 205 | 112 |
| 3. Hepatocellular carcinoma | 18 | 3 |
| Total | 225 | 376 |

Each of these patients also received chemotherapy (Docetaxel), in addition to immunotherapy (Bevacizumab). There were measurable shrinkages of the tumor burdens, as well as improvement in the quality of life of the remaining 66 patients. Only seventeen (17) of the patients who received Bevacizumab are still alive as at 31st July, 2020. The 238 patients with metastasis, who could not afford immunotherapy, had a more rapid, downward course in survival and in their quality of life, chemotherapy notwithstanding. One hundred and seven (107) of them died in hospital, while the remaining 131 (out of the 238 patients) were lost to follow-up.

Discussion

Different types of cancers have different biological propensities. Some cancers metastasize early while others metastasize late, depending on the grade of the cancer. Those that metastasize early are the anaplastic cancers which are so much in a hurry to spread, such that they do not have enough



time to arrange their cells into any semblance of the type of tissue of origin. In breast cancer, for example, they display a very high Ki-67 Proliferative Index. This is associated with high grade of tumor, aggressive attitude of tumor, poor survival of patients, early recurrence of tumor, and metastasis [10].

Many more females were reflected in this Study because majority of our patients were females with carcinoma of the breast. A few of them also had colorectal carcinoma. Majority of the male patients had colorectal carcinoma, with just two cases of carcinoma of the breast in males (an 84-year old retired civil servant, and a 42-year old trader).

The only female patient, a Nun, who was able to take Bevacizumab 3-weekly for 12 courses, had Triple Negative Cancer of the left breast, with metastasis to the lungs. She is one of the 17 survivors. None of the other sixteen patients had Triple Negative or Her2 Positive breast cancer. We think that the 131 patients who were lost to follow-up may have died at home or, may have died in other health facilities.

Many previous studies¹⁻⁴ have shown that immunotherapy has the ability to increase survival rate and quality of life of patients, as well as to reduce the rate of recurrence of cancer. Combination of chemotherapy with immunotherapy, as in this study, has also been shown by previous studies [8-10] to enhance survival of patients.

Conclusion

We conclude that immunotherapy has a beneficial effect in metastatic cancers. This beneficial effect is enhanced by the combination of chemotherapy with immunotherapy, and by repeated doses of this combination.

Recommendations

Reduction in the price of immunotherapeutic agents will enable more patients to acquire these truly priceless drugs.

The federal government's National Health Insurance Scheme (NHIS), as presently packaged, should be modified to cover patients with cancer.

Further studies will be needed in our Centers, to objectively look at the effect of immunotherapy alone, compared with chemotherapy alone, in the treatment of metastatic cancers.

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