Second Malignancy in a Patient with Long Survival from Solitary Plasmacytoma Previously Treated with Radiation

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Abstract: We report a case of a 39 year- old man with second malignancy 13 years after chemo-radiation therapy for solitary plasmacytoma of the fontal bone. The risk of second cancers is a well-known adverse late effect of radiation therapy. However, this risk may be less with the use of proton-beam therapy, the patient actually presented with nasal bleeding of 5 years duration and progressive swelling of the face of 2 years duration with associated nasal obstruction and weight loss. Examination revealed a bilateral purulent conjunctival hyperemia .Direct examination revealed swelling on the frontal sinus and swelling over the antrum. CT brain showed malignant and vascular tumor of the frontal bone involving the nasal bones and paranasal sinuses and compressing the frontal brain tissues. This was histologically confirmed. The frontal bone was completely destroyed and frontal brain tissue was covered only by skin. He received 6 courses of 3 weekly combination chemotherapy with total of 60Gy of radiotherapy to the left and lateral face and 10Gy to the anterior face with complete regression. He was on follow up for 3 years during which the lesion was controlled with no evidence of recurrence nor neutral deficit. Patient was however lost to follow up for 10 years. He presented again after 13 years of treatment with complaints of painful ulcer on the right lower mandible and biopsy of lesion came as squamous cell carcinoma. This was completely different from the firs histology of plasmacytoma for which he received external beam radiotherapy, however the site of present disease was in the field of previous treatment. This is therefore suggestive of a second malignancy appearing 13 years after the initial external beam radiotherapy. He received cisplatin and 5fluorourasil in preparation for further radiotherapy after chemotherapy patient lost to follow up again and eventually was confirmed to have died at home.
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Background:

Plasma cell neoplasms represent a spectrum of diseases characterized by clonal proliferation and accumulation of immunoglobulin (Ig) – producing terminally differentiated B cells[1]. Plasmacytoma comprise < 10% of plasma cell dyscrasia[2].

There are two types of plasmacytoma: solitary and Extramedullary plasmacytoma. Solitary plasmacytoma is the localized diseases that can arise from the bone while extramedullary plasmacytoma arise in the soft tissue[3].

Solitary or multiple extramedullary plasmacytomas have been described in the liver, spleen, lymph nodes, kidneys, subcutaneous tissue and brain parenchyma.

The incidence rate rises with advancing age, with a median age at diagnosis of 70 years and < 1 % of cases are diagnosed in persons < 35 years, for plasma cell myeloma while the median age at diagnosis of solitary plasmacytoma is 55 to 65 years, on average about 10 years younger than patients with multiple myeloma[4, 5] males are affected predominantly (male: female ratio 2:1[6]. Solitary plasmacytoma requires specialized techniques for accurate staging, including a CT scan and MRI to exclude more disseminated disease[1].

A monoclonal protein in the serum is observed in 24% to 54% of patients, but in the remaining cases no detectable monoclonal protein is seen, even on immunofixation. Extramedullary plasmacytomas are diagnosed less frequently and require a work up, including MRI and positron emission-tomography to rule out additional sites or disseminated disease.

In solitary plasmacytoma, the diagnosis is established when a solitary lytic lesion is shown by needle or surgical biopsy to be composed of plasma cells and marrow aspiration from a distant site contains less than 5 percent plasma cell[7]. Extramedullary plasmacytoma on biopsy is composed of plasma cells.

Case Reporting

A 39 year old man who was referred to Radiotherapy clinic, University College Hospital, Ibadan with 5 years history of recurrent epistaxis, progressively worsening. He presented with nasal

bleeding of 5 years duration and progressive swelling of the face of 2 years duration (in Nov. 25, 1997) with associated nasal obstruction, weight loss and anorexia. Examination revealed a young man, not pale, bilateral purulent conjunctival hyperemia. Direct examination revealed swelling on the frontal sinus, soft fluctuant, non-pitting extending over the hair margin, fullness and obliterating of the nasal bridge involving the median canthus. Swelling over the antrum, soft, non-pitting, non-tender with trismus.

NOSE

Pale, fleshy mass obliterating both nasal cavities within the vestibule.

ORAL CAVITY

Trismus, Good oral hygiene, no loosening or loss of teeth

Cranial Nerves

1 – anomic

6- palsy

Other systems were within normal limit.

Hematological, Biochemical and Radiological work up including FBC, E&U,CR, LFT, clotting profile, Retroviral Screening, CT Brain all showed Normal except CT Brain that showed malignant and vascular tumor of the frontal bone involving the nasal bones and para nasal sinuses, and compressing the frontal brain tissue. The frontal bone was completely destroyed and frontal brain tissue was covered by only the skin. He had biopsy and histology came out to be Solitary plasmacytoma. He received 3 weekly combination chemotherapy with vincristine, Adriamycin and cyclophos phamide x 6 courses and Radiotherapy total of 60Gy to Right and Left lateral face and 10Gy to the Anterior face between 28-11-97 to 12- 1-1998. And 30Gy to the Right Anterior face between 15 – 11 – 99 to 2 – 12 – 1999 with remarkable tumor regression and improvement in a patients' daily activities, pain was controlled with analgesics. Patient was seen on follow-up for 3 years (1999- 2002) during which the lesion was observed to have regressed with no neural deficit, because of the vulnerability of the frontal brain to injury he was advised to put on helmet when outside the house. Patient was however lost to follow-up for 10 years and showed up this years with no recurrence on the primary site. New frontal bone was noticed to have been formed and patient general health was stable with no central nervous system symptoms.

Patient however complained of painful ulcer on the right lower mandible and biopsy was taken and report come as squamous cell carcinoma. This was completely different from the first histology of plasmacytoma for which he received external Radiotherapy however the site of present disease was in the field of previous treatment. This is therefore suggestive of a second malignancy appearing 13 years after the initial external Radiotherapy. He has since been commenced on chemotherapy viz cisplatin and 5 fluorouracil in preparation for further Radiotherapy.

Hematological, Biochemical and Radiological work up including FBC, RVS, E&U,CR, Skull, Jaw and Chest X – Ray showed normal.

Pain controlled on analgesic.

Discussion

Plasmacytoma comprise < 10% of plasma cell dyscrasia. Less commonly solitary plasmacytoma presents in an extramedullary site (20%) usually as a mass in the upper aero respiratory passages that produces local compressive symptoms[5, 6, 8]. It increases with advancing age. Generally they are all highly radiosensitive[3] many cases are reported in literature of high rate 5 years survival. Radiation therapy is the standard treatment for solitary plasmacytoma. Surgery is consider for bone instability fractures, or when there is rapidly progressive neurologic deterioration such as spinal cord compression[10,11].

This patient presented with a large tumor with good disease control which is not similar to OZsahin et al.[11] that reported that local control was better with small tumors{<4cm} in patients treated with radiotherapy. Solitary plasmacytoma are radiation – sensitive tumors. The patient received high grade radiotherapy which is similar to OZsahin et al that reported that higher dose can be given to improve local control.

This patients presented with 5 years history of recurrent epistaxis, and 2 years history of progressive facial swelling with associated nasal obstruction. Because of the geographical location of the tumor, surgery could not be done. The benefit of chemotherapy, either alone or in combination with radiotherapy and surgery, as primary therapy has not been proven[2]. Moreover, the benefit of adjuvant chemotherapy given to prevent recurrent disease and or progression to myeloma is also undefined.

A recent report suggest that the disappearance of protein after involved field radiotherapy predicts for long-term diseases free survival and possible cure[9]. Long-term follow-up is require for all patients treated for solitary plasmacytoma of bone and extramedullary plasmacytoma. More than 50% of cases with solitary plasmacytoma of bone progress to multiple myeloma at 5 years (KNOBEL et al 2006), and approximately 15% of patients with extramedullary plasmacytoma progress to multiple myeloma at 10 years after treatment (Aleqxiou et al 2000). In UCH cancer registry over a period of ten years, we saw a total of 12 cases of Plasmacytoma (10 male, 2 female). Radiation exposure is a well-

established risk factor for developing second malignance neoplasm, estimating the true incidence of radiation-induced second malignance neoplasm is difficult. This is due to the fact that, in addition to radiation exposure, the genetic abnormalities (e.g., Li-Fraumeni syndrome) and risk factors associated with primary tumors (e.g., smoking) could predispose the individuals to develop a second cancer[13, 14]. Radiation induced second malignance neoplasm has also been observed at high doses of radiation of up-to 45Gy[15], although this patent received up to 60 Gy which was high dose. The development of second malignance neoplasm in patients treated with radiotherapy has been reported to follow a similar timeline of 10-60 years for solid tumor[16, 17, 18, 19, 20]. This patient had second malignance in the oral cavity thirteen years after initial treatment. Multiple epidemiological studies have confirmed the importance of age in predicting second malignance neoplasm risk at the time radiation exposure. For the same dose, patients exposed to radiation during childhood are at a significantly higher risk for developing second malignance neoplasm compared to those exposed at older age[21, 22]. This patient was thirty nine years old when he received initials radiotherapy. Radiotherapy and chemotherapy are associated with an increased risk of second malignant neoplasm after cancer treatment according to Guerins et al. Patients receive both chemo and radiotherapy together.

Conclusion

The local control can be achieved in this disease with chemo-radiation, it was not however clear if the second malignancy was due to the radiotherapy but there was a suspicion because the previous radiotherapy field was inclusive of the site.

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