Case Report: Treatment of metastatic germ cell tumor in a newly diagnised HIV infected man: use of BEP chemotherapy.

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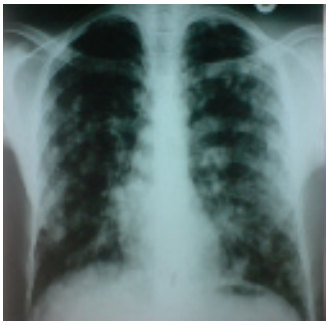
Introduction

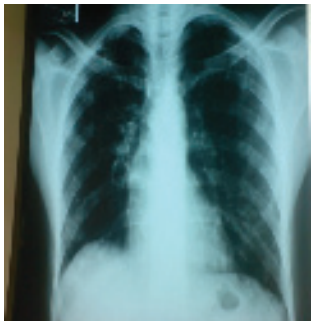
Case history

A 29 year old man presented in August 2010 at with 3 month history of abdominal pain, 3 week history of testicular swelling and abdominal mass. He also reported cough and weight loss. Patient had been working as water proofer for the last 8 years, single and fathers of an 18 month old child. He has no family history of malignancy, is a heavy drinker (45 units per week) but non-smoker. On examination he looked wasted, in obvious pain, dyspneic with a respiratory rate of 40/min. He had cervical lymphadenopathy , moderate gynacomastia, a central abdominal mass of 10×8 cm and right testicular mass. The chest had diffuse crepitations; the rest of the examination was unremarkable. Chest radiograph revealed diffuse widespread infiltrates in both lung fields (See fig.1A). The admitting medical officer suspected TB. Sputum for AAFB was negative and CT scan of abdomen revealed para-aortic mass measuring 9X12 cm (see fig.2A) with right hydronephrosis (see fig.3A), patient initially refused hiv testing but at a later stage tested positive using Unigold (rapid hiv -1 antibody test), base-line CD4 count was 331 cells/μL, kidney function was normal, normal liver enzymes: ALP103.9iu/l, AST35.1iu/l, ALT9.1 iu/l, LDH 2192.7. At one week from initial presentation, evaluation and consultation with the oncologist on the clinical picture and results changed the diagnosis of TB and testicular cancer was suspected. We were unable to measure α-fetoprotein (AFP)and b-hCG at base-line ,further review of the chest xray showed cannon ball in both lung fields. The findings of a testicular mass, abdominal mass and cannon balls on the chest xray were much more in keeping with a testicular cancer with metastases to the lungs .



(Figure 1A)

Fig: 1a Diffuse widespread infiltrates on both lung fields before chemotherapy



(Figure 1B)

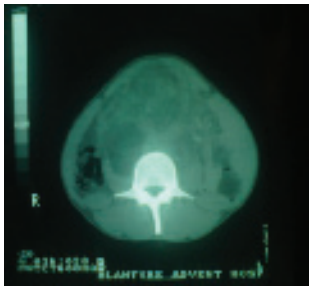
Fig: 1b Complete resolution of lesions in lung fields after chemotherapy

This is a Testicular cancer suspect with lung metastases initially thought to be TB who refused an hiv test

What would be your approach to management ?

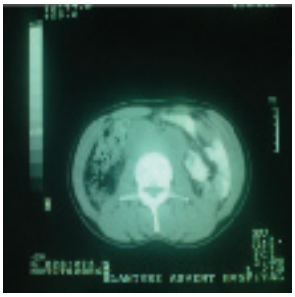
Treatment

An orchidectomy of the right testis was performed and histology revealed yolk sac tumor which is a type of a germ cell tumor (GCT). After the surgery, four cycles of BEP (Bleomycin 30 IU weekly i.v, etoposide 100mg/m2 D1-5 p.o and cisplatin 20mg/m2 D1-D5 i.v) in 21 day cycles over a period of 3 months were given. The hematological counts and renal function were closely monitored throughout his treatment. Whilst on treatment, he was transfused 3 units of packed red cells and had a course of granulocyte-colony stimulating factor (Filgrastim) to treat severe neutropenia . He had renal dysfunction on two occasions with his creatinine being 1.79mg/dl and 5mg/dl respectively. This prompted a delay of cisplatin administration but not Bleomycin and etoposide, aggressive fluid diuresis and recommencing cisplatin only with normalization of creatinine clearance. During the third BEP cycle patient developed malaria confirmed by blood film parasetemia of 2+. He was put on antimalarial treatment-Lumefantrine Artemether for three days to which he responded.



(Figure 2A)

Fig 2a abdominal bulky mass measuring 9X12 cm before chemotherapy



(Figure 2B)

Fig 2b Two masses showing tumor regression with central necrosis 3x3cm & 3x2.5cm in size after chemo

The patient's chemotherapy was delayed once for severe neutropenia. After 4 BEP cycles, patient had responded well to chemotherapy: abdominal mass was not palpable and had only a residual mass detectable on abdominal CT scan (Fig 2b). Chest radiograph showed clearing of cannon balls in lung fields (see fig.1b) and the abdominal CT scan findings of tumor regression with central necrosis were consistent with remarkable response(see fig. 2b), beta-hCG was 11.[1] mIU/ml and AFP 24 ng/ml. In the course of chemotherapy the patient subsequently accepted an HIV test,CD4 was as above . This same time cotrimoxazole prophylaxis was commenced. Patient was stable, orchidectomy scar healed and was commenced on Triomune (HAART) soon after finishing his chemotherapy due to delayed HIV testing.

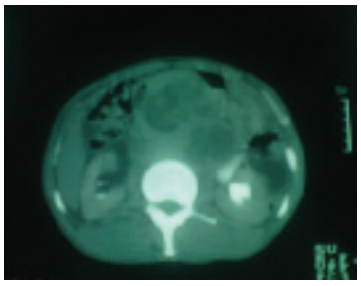
Discussion

It is estimated that about 40% of HIV infected patients will develop a malignancy at some point in their life[1]. Germ cell tumors are known to appear more frequently in HIV infected patients and with high HIV prevalence in Malawi, it is important to examine the management of such malignancies. The exact management of germ cell tumors in general in HIV patients remains an area of uncertainty and is challenging. Three main reasons are suggested. First being HIV causing mortality due to opportunistic infections[2]. Secondly, HIV infected patients tolerate chemotherapy poorly resulting in dose reductions that entail lower response rates which did not happen in our patient[2]. Thirdly, HIV patients have more aggressive tumors or intrinsic chemotherapy resistance.[3,4,5] Our patient presented with metastatic disease and bulky intra-abdominal nodes which under-pins aggressive disease in this group of patients. Some reports suggests management of such patients with concurrent HAART and chemotherapy to improve treatment effectiveness.[6,7] The improved survival that ensures is probably due to decreased HIV related mortality and better chemotherapy tolerance[8,2]. However other studies suggest that HIV-positive patients do not have excess toxicity compared to historical HIV-negative controls[9,10,11]. This suggests that poor outcome in HIV infected GCT is a result of HIV complications mostly opportunistic infections.

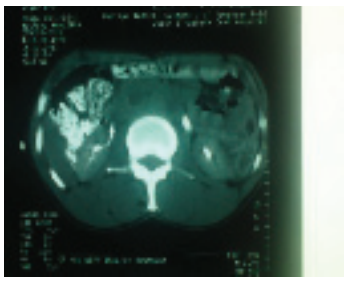
BEP a well tolerated and effective first line treatment for metastatic germ cell tumors, more specifically seminomas,which offers good survival and prognosis was used in this patient[7]. It is common for patients to have residual necrotic masses after chemotherapy for bulky disease, which was the case in our patient. It has been noted that complete responders may have such residual masses. A residual mass of <3 cm and a poorly defined residual mass of ≥3 cm can be observed, reserving intervention for recurrent or progressive disease. Well-defined residual masses of ≥3 cm should be resected because there is a 55% likelihood of persistent disease. There was no immediate indication to intervene in the residual necrotic mass in this patient that was about 3 cm.

In our patient, the respiratory symptomatology and CXR findings were initially mistaken for TB (See Fig1). It is not everything that looks like TB that is TB. Malignancies in a region that has high TB prevalence may easily be mistaken for TB as was this case. The patient was given cotrimoxazole prophylactic cover 480 mg twice a day, standard chemotherapy which was successfully delivered and a good treatment response obtained. This is more relevant in any setting where accessibility to ARVs is challenging because of long waiting lists. Hence this strategy would allow the cancer treatment for GCT be delivered without being delayed by the wait for HAART commencement. According to WHO recommendation, if the HIV test and base-line CD 4 count of our patient (<350 cells/μL) was done before initiating chemotherapy, he would have qualified for HAART upfront. The refusal to test HIV offered a unique opportunity to observe a different strategy from the recommended concurrent approach of HAART and chemotherapy. BEP still offered remarkable response in the patient despite HIV positivity, being ARV naïve, advanced metastatic lung lesions and bulky abdominal disease(Compare Fig :2a and Fig :2b).

However, despite the initial response to chemotherapy, the response was not durable as the patient suffered lung relapse 5months after completion of chemotherapy. This could be as a result of initial high disease burden/bulky disease and aggressive disease in an HIV positive individual. The second explanation for this un-durable response may be the delays in delivering adequate doses of chemotherapy due to the episode of renal dysfunction and on another occasion due to neutropenia.



(Figure 3A)



(Figure 3B)

Fig :3a hydronephrosis in right kidney before chemo
Fig :3b resolved hydronephrosis after treatment

We suggest not delaying BEP in those with CD 4 count <350until HAART commencement where HAART is difficult to access or patient fails to consent either for HIV

testing or initiating HAART itself. This case demonstrates it is feasible to deliver treatment using non-concurrent approach.

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