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RESIDUAL MASSES IN RETROPERITONEUM AFTER CHEMOTHERAPY IN NONSEMINOMATOUS GERM CELL TUMOURS OF TESTIS - SINGLE INSTITUTIONAL STUDY - REVIEW OF 14 CASES.

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Background: It is well recognized that Cisplatin based Chemotherapy is highly effective in metastatic testicular cancer. Non Seminomatous Germ Cell Tumours (NSGCT) & it's metastasis are most chemosensative cancers. Most cancers become systemic when spread to Lymph nodes. There fore involved lymph node removal is not curative, because there are micro metastasis at distant places. The spread of testis cancer is different i.e.it is by & large more predictable and sequential. Hence surgical treatment of Residual masses in Retroperitoneum is curative in 35 to 75 % of patients. In this original article we want to present our study of fourteen cases of "Significant Residual disease "in Retroperitoneum and in two cases in Mediastinum, after Cisplatin based chemotherapy for NSGCTs by doing Retroperitoneal Lymph Node Dissection (RPLND) in all fourteen patients, along with Simultaneous Mediastinal Lymph node dissection (MLND) in one patient, and elective in one patient. With Primary Teratoma of Mediastinum along with Bilateral pulmonary metastitectomy. **Aim:** Aim of this manuscript is to review the role of RPLND in post chemotherapy patients in a single institutional study of 14 patients. **Methods:** This single institutional on going longitudinal study at tertiary care teaching institute started in 2009, since then we had 14 patients included in the study. Selection criteria was defined and the findings were recorded in prestructured prosoma. **Results:** We had 14 patients, all received Cisplatin based chemotherapy for high tumor burden in the retroperitoneum, marked by Imaging & Tumor Markers with no significant response, marked by reduction in size of masses in retroperitoneum, nor levels of Tumor markers. All patients belonging to the age between 18 to 27 years. Standard bilateral template RPLND done in all patients with one patient subjected for simultaneous RPLND & Mediastinal Lymph node dissection. There was no operative or Post operative mortality. Morbidity noted in terms of Post operative Prolonged Ileus, Lymphorroea through drain, and one patient had retrograde ejaculation. **Conclusion:** Post chemotherapy RPLND is definitely challenging as there is lot of Desmoplasia.. 9 out 14 patients are in follow up show no evidence of relapse of disease, 3 of them, were we could do nerve sparing RPLND are happy with the marriage life. Sperm banking was done only in three patients - have children. There was no mortality but morbidity is seen in postoperative period. **Inclusion Criteria**: Patients with diagnosis of NSGCT treated with Platinum based Chemotherapy. Who recovered completely from effects of Chemotherapy in terms of WBC, Platelets, LFT, PFT, KFT, No extra pulmonary Metastasis. Post chemotherapy significant residual masses in retroperitoneum as on Imaging compared to pre chemotherapy tumor load, with high levels of tumor markers. Patients who are willing to enroll in this study **Exclusion Criteria**: Patients with evidence of Extra Pulmonary Metastasis, Patients with Poor Lung function after Bleomycin based chemotherapy. Not willing to enroll in this study.

KEY WORDS: NSGCT, Cis-Platinum -Chemotherapy, Residual Masses Tumor markers, CT Scan, RPLND.

INTRODUCTION

The advent of Platinum based chemotherapy has had a major impact on both the timing and the technical requirements of RPLND. NSGCT occur in young patients, majority are treated with High orchiectomy. Then stage of the disease and level of Tumor markers guide us the further treatment of the disease. We want to go evidence based and show that the Significant Residual disease in Retroperitoneum & even in Mediastinum after Chemotherapy should not discourage clinician. One should aggressively treat the disease by doing RPLND and MLND either simultaneously or electively depending on patient's fitness, infrastructure available, anesthesia facilities.

If there are residual masses after chemotherapy in NSGCTs There is no method by which you know the Histopathology of these masses. The CT, MRI, even PET

can only tell you about presence of mass, but no information weather it is residual tumor, mature Teratoma , necrosis, or Fibrosis can be gathered. With Salvage chemotherapy, outcome is not very good. So we treated the disease aggressively, following the criteria given in literature.

METHODS AND MATERIALS

We started this study from December 2009 onwards, This is on going study with review of 14 patients.

We have treated fourteen patients between the ages of 18 to 27yrs of age. All of them have received four cycles of Cisplatin, Etoposide, Bleomycin chemotherapy for high burden of NSGCTs, confirmed by High levels of tumor markers and Imaging by CT scan. Out of fourteen patients one boy of 18 years had Mediastinal Teratoma along with isolated bilateral Pulmonary Metastasis after RPLND done Six months back, & he receieved, Salvage Chemotherapy- He was considered for Excision of Mediastinal mass with MLND and pulmonary metastectomy.

We assessed these patient s by doing Levels of AFP, beta HCG and LDH and if these levels are near normal or less than 3 fold increase, & CT scan suggests that the masses are reduced < 90% or the size of Lymph nodes–if more than 1.5 to 2cms. After chemotherapy, and most importantly no extra pulmonary metastasis. These patients are then considered for RPLND. But as these patients receive chemotherapy we take care that Blood picture is normal, and Pulmonary Functions comes to normal. Because these patients receive Bleomycin as Chemotherapeutic agent which causes pulmonary fibrosis, so anesthesiologist must be very careful about giving fluids, and maintaining FIO2 as it may result in oxygen toxicity or fluids can cause acute Pulmonary edema.

Surgical Technique

Preoperative preparation of patient, we keep ready sample bottles with proper labelling for collection of samples of various levels of lymphatic tissue. Anesthesia by experienced anesthetist by keeping a close watch on FIO2 & fluid infusion.

We used standard trans abdominal open approach with reflection of bowel from ileocaecal junction to Ligament of Trietz, reflected up with entry in to Retroperitoneum & use the dissection limits - removal of lymphatic tissue between both ureters, starting from the crus of diaphragm to the bifurcation of the common iliac arteries. In the era of Laparoscopy many centers are trying Laparoscopic technique but I personally have preferred open method with fear of Injury to important structures because of Desmoplasia. I may prefer it for primary RPLND if required. As we refined our technique of RPLND we did three nerve sparing RPLND but rest 11 patients we failed to do may be because of Desmoplasia.

REASULTS

As on now it is almost more than 8-9 years, we operated our first patient and following other patients since last 8-9 years. we follow them initially by doing CT scan Abdomen, Chest & with Tumor markers every 6 months for 2 years & then every year. Till now we had 9 patients coming for follow up with absolutely no residual disease or relapse. We lost two patients one with bilateral Pulmonary Mets were persistent rise in tumour markers - and another young man after 6 years had metastasis in Liver. In routine we did not see any relapse at the local site after the modified Template bilateral RPLND in Post chemotherapy scenario, (Debono D.J.et al j.Clinical oncology 15:1-1455 1464-1997.) local site relapse rates are < 5%.

In our patients we had no operative or post operative mortality. There was problem of Lymphorrea in 3 patients were we did simultaneous RPLND & MLND and prolong ileus, which was treated with low fat diet prolong Nasogastric Intubation & IV alimentation. Though there was lot of Desmoplasia with chemotherapy there was no Injury to major structures, except in 1st patient we had a a injury to infrahilar vena cava, which was repaired immediately. Recovery in all patients was uneventful, no anesthesia complications noted, in post operative period.

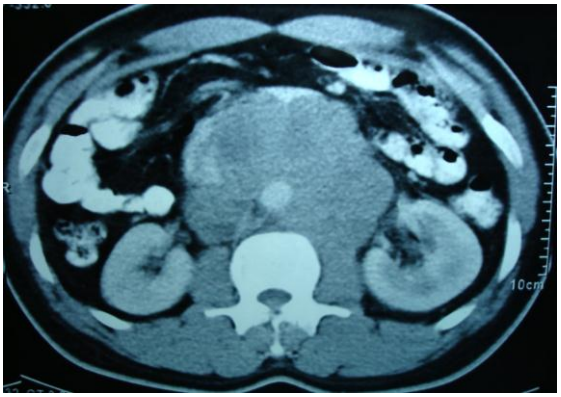
There was an problem associated with one young boy who had only MLND with resection of Bilateral Pulmonary mets, was -Tumour markers Rising after 3 months again so probably the disease was aggressive/ inadequate resection, we follow these patients every six months- Tumor markers, CT scan, we have received one patient with Retrograde Ejaculation, because all our patients already had chemotherapy and so there was lot of Desmoplasia and difficult to see those nerves of ejaculation.

CONCLUSIONS

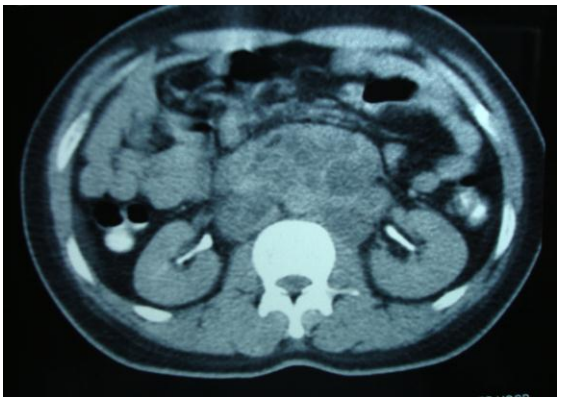
Treatment of residual masses after Chemotherapy either in Retroperitoneum/ in Mediastinum attracts surgeons attention.

Not all patients need RPLND Observation after chemotherapy in selected cases is an evidence-based strategy. (kregeS. et al our Uro 53-478-496-2008)

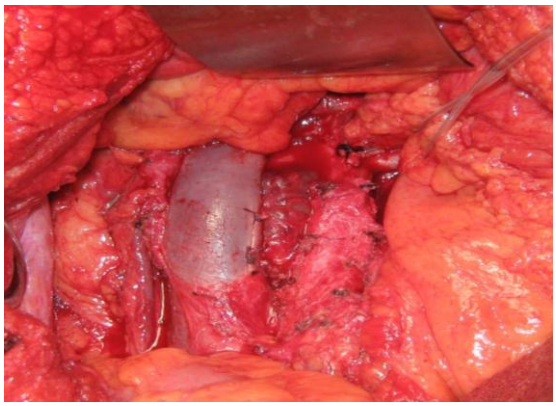
Imaging of Retroperitoneum, Chest & Abdomen and Tumor markers are of utmost importance as far the decision of Observation /surgery is to be made.



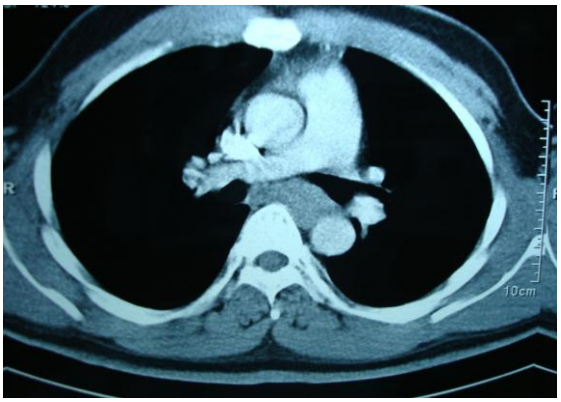
Pre Chemotherapy mass in retroperoneum



Post Chemotherapy Residual Mass in Retro Peritoneum



Intraoperative -Inter aortocaval Lymph node.

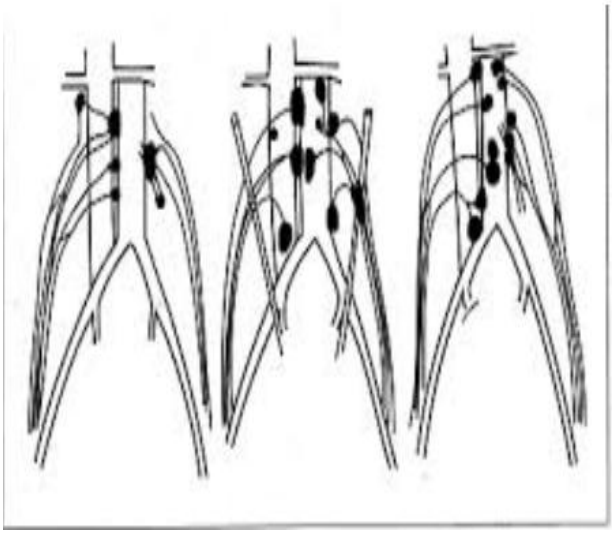


Mediastinal Mass in Testicular NSGCT.

Basic aim of RPLND in selected patients, is diagnostic as well as Therapeutic because there is no investigation available (Even PET Scan) which tells you accurately that the residual mass is containing the residual tumor, necrosis, mature Teratoma or a fibrosis.

RPlND not only evaluates response of chemotherapy which no other investigation gives, But in selected patients it reduces the tumor burden and helps in deciding about Salvage Chemotherapy

Our small work concludes with the fact that RPLND should be done for residual masses in NSGCT in appropriately selected patients, with due care, for chance of cure, to know the Histopathology of disease, and if needed further chance of Chemotherapy.



Modified Template for Bilateral dissection in post Chemotherapy Scenario

Foot Notes – NSGCT- Nonseminomatous Germ cell Tumors, RPLND- Retroperitoneal Lymph node Dissection, MLND- Mediastinal Lymph Node Dissection. LDH- Lactose Dehydrgenase, AFP – alpha fetoproteins, Beta HCG- beta Human Chorionic Gonadotrophins. PET- Positron Emission Tomography.

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