Assessing Response to Chemotherapy in Bone and Soft Tissue Sarcoma

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Multidisciplinary Approach

• Neoadjuvant chemo is a well established tactic is the treatment of sarcomas

• Tumor response is assessed by radiologic & histologic means

• Teamwork
Radiologic Assessment

• MRI is the radiologic modality used to assess response of sarcomas to preoperative chemotherapy.

• The radiologist evaluates tumor size, peritumoral edema, and necrosis
Limitations

• MRI estimation of tumor necrosis does not always parallel histological examination

• Changes in tumor size difficult to integrate into a response scoring scheme, because cystic transformation, hemorrhage and necrosis can lead to an increase in size although the tumor is responding
Histologic Assessment

- The pathologist gets the actual tissue.
- Can assess tumor necrosis more reliably.
- Histologic assessment of necrosis has been standardized in bone sarcomas because this is one of the best indicators of prognosis.
Examination of a Bone Tumor Resection

Bivalve specimen ➔ obtain a slab ➔ fix in formalin ➔ decalcify for few days ➔ sample slab completely ➔ Histologic examination
Histologic Assessment

The Huvos system is based on % tumor necrosis:

- Grade 1: Necrosis < 50%
- Grade 2: necrosis of 50%–90%
- Grade 3: necrosis between 90%–99%
- Grade 4: 100% necrosis

Applies to both osteosarcoma & Ewing sarcoma
Practical Cutoff Percentage

• 90% necrosis or greater = Good response
• Less than 90% necrosis = Poor response

Acellular spaces (necrosis)

Tumor osteoid
DIAGNOSIS:
RIGHT DISTAL FEMUR, LIMB SALVAGE RESECTION:
- MALIGNANT FIBROUS HISTIOCYTOMA OF BONE, WITH 30% TO 40% TUMOR NECROSIS, INVADING LATERAL & POSTERIOR PERIOSEOUS SOFT TISSUE.
- FREE BONE SURGICAL MARGIN (4 CM AWAY FROM TUMOR).
- FREE SOFT TISSUE MARGIN WITH A CLOSE LATERAL MARGIN (0.1 CM AWAY FROM TUMOR).
How about Soft Tissue Sarcoma?

• Currently, there are no standard techniques for the pathologic evaluation of pretreated soft tissue sarcomas.

• Still unclear whether cut-off for prognostic relevance is similar in the many different histological subtypes of STS.
Proposed Method

• Task force sponsored by the European Organization for Research & Treatment of Cancer – Soft Tissue & Bone Sarcoma Group (EORTC–STBSG) proposes a standardized method for pathological examination process and the reporting of STS resection specimens.
From OR to the Path Lab

• Orient the specimen
• Transport intact and unfixed resection specimen ASAP
• If direct transport to pathology not possible within a few hours, fix in formalin
Gross Examination

- If specimen orientation unclear, the surgeon is contacted
- Surgical margins are inked
- Specimen is sliced into 1 cm thick slabs

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Gross Examination

• One representative complete central slab is selected and embedded entirely in a grid-manner
Histologic Examination

- Grading of the tumor is no longer possible if post neoadjuvant treatment
- Therapy response is expressed as percent tumor necrosis
- Many studies have employed a $\geq 95\%$ necrosis cut-off point for designating good and poor response to therapy
- In addition to necrosis, other tumor changes can also be related to treatment
Other Histologic Changes Related to Neoadjuvant Treatment

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Take Home Points

• Histology > Radiology in assessing response
• % necrosis as measured histologically is one of the most important prognostic factors for localized osteosarcoma. Cutoff is 90%.
• Histologic assessment of tumor necrosis requires extensive sampling
• Currently, no standard techniques for the pathologic evaluation of pretreated soft tissue sarcomas.
Children from the Children's Cancer Center of Lebanon on stage with Lebanese singer Cyrine Abdelnour, at the fundraiser organized by LAU students.
Thank You