RADIOTHERAPY IN ACUTE LEUKEMIAS
RADIATION THERAPY IN ALL

- PROPHYLACTIC CRANIAL IRRADIATION
- THERAPEUTIC CRANIAL IRRADIATION
- THERAPEUTIC CRANIAL AND NEURAXIS RADIATION
- TESTICULAR IRRADIATION
- MEDIASTINAL IRRADIATION
- TOTAL BODY IRRADIATION – BMT CONDITIONING
DEFINITION OF RISK GROUPS
ALL BFM 95

• STANDARD RISK (6 CRITERIA)
• PREDNISONE GOOD RESPONSE (BLASTS <1000 /MICROLIT OF PERIPHERAL BLOOD ON DAY 8) AFTER A 7 DAY PREDNISONE PREPHASE (PRED-GR)
• WBC <20,000/MICRO LIT AND AGE >1-<6 YEARS
• A COMPLETE REMISSION ON DAY 33 (M1-MARROW)
• NO TRANSLOCATION t(9:22) OR BCR/ABL RECOMBINATION
• NO TRANSLOCATION t(4:11) OR MLL /AF 4 RECOMBINATION
• NO T – IMMUNOLOGY
MEDIUM RISK GROUP
(4+1 or more)

• LEUKEMIC CELLS <1000/MICROLIT IN THE PERIPHERAL BLOOD ON DAY 8(PREDNISONE–GR)
• COMPLETE REMISSION ON DAY 33(M1-MARROW)
• NO TRANSLOCATION t (9:22) OR BCL/ABL RECOMBINATION
• NO TRANSLOCATION t(4:11) OR MLL/AF 4 RECOMBINATION
• LEUKOCYTES MORE THAN 20,000 /MICROLIT, AGE LESS THAN ONE YEAR OR MORE THAN 6 YEARS
HIGH RISK GROUP (EVERY CRITERION)

- MORE THAN 1000/ MICROLIT LEUKEMIC CELLS IN PERIPHERAL BLOOD ON DAY 8 (PRED=PR)
- NO COMPLETE REMISSION ON DAY 33
- TRANSLOCATION t(9:22) OR BCR/ABL RECOMBINATION
- TRANSLOCATION t(4:11) OR MLL/AF4 RECOMBINATION
DEFINITION OF CNS STATUS

• CNS STATUS 1(NEGATIVE):
  •
  • NO CLINICAL EVIDENCE OF A CNS DISEASE
  • NO IMAGING-CT/MRI -EVIDENCE OF CNS LESION
  • NORMAL FUNDOSCOPIC FINDING
  • BLAST FREE CSF
DEFINITION OF CNS STATUS

• **CNS STAUS 2 (NEGATIVE):**
  
  • BLASTS UNAMBIGUOUSLY IDENTIFIED, RBC:WBC <100:1 ON CYTOPSIN PREPARATION OF CSF WITH A CELL COUNT OF <5/MICROLIT- NON TRAUMATIC UN CONTAMINATED CSF

• BLASTS IDENTIFIED, RBC:WBC >100:1 ON CYTOPSIN PREPARATION OF CSF- TRAUMATIC BLOOD CONTAMINATED CSF

• TRAUMATIC LP (BLOOD CONTAMINATED CSF)
DEFINITION OF CNS STATUS

• **CNS STATUS 3(POSITIVE)**
• A MASS LESION IN THE BRAIN AND OR MENINGES ON CT/MRI
• CRANIAL NERVE PALSY UNRELATED TO OTHER ORIGIN EVEN IF THE CSF IS BLAST FREE OR NO CIRCUMSCRIBED SPACE OCCUPYING LESION ON MRI/CTSCAN
• PURE RETINAL INVOLVEMENT WITH BLAST FREE CSF AND NO MASS ON CT/MRI
• NON TRAUMATIC LP WITH A CSF CELL COUNT OF >5/MICROLIT
CRANIAL PROPHYLAXIS - ALL

**ALL-BFM 83** - 12 GY OF PREVENTIVE CRT WAS AS EFFECTIVE AS 18 GY OF HIGH-SRG

**ALL-BFM 90** - REDUCTON OF LONG TERM MORBIDITY IN PRED-GR PATIENTS BY LIMITING RADIATION DOSE -12 GY TO MR-ALL AND HR

**ALL -86 TO 90-IN CRITICAL GROUPS INCIDENCE OF CNS RELAPSE WAS LESS THAN 5 %. ESPECIALLY WITH HD-MTX AND MTX -IT INCIDENCE WAS LESS THAN 3 %

**ALL-BFM-90**-12 GY INSTEAD OF 18 GY PROVIDED EQUALLY EFFICIENT CNS PROPHYLAXIS IN HIGH RISK GROUPS HAD PGR

**AMERICAN STUDIES** –MR PATIENTS WITH T-ALL HAD HIGHER INCIDENCE OF SYSTEMIC AND CNS RELAPSE IN NON IRRADIATED PATIENTS

ALL-BFM 95
CRANIAL PROPHYLAXIS

- CHILDREN AND ADOLESCENTS < 18YRS) WITH MEDIUM RISK GROUP WITH T-ALL AND ALL HIGH RISK GROUP PATIENTS
- NO RT FOR STANDARD RISK AND MEDIUM RISK PATIENTS (EXCEPT T-ALL)
- DOSAGE: AGE - LESS THAN ONE YEAR - NO RT
  AGE - ONE YEAR OR MORE - 12GY
- ADULT PROTOCOLS - 18 TO 24GY
CRANIAL IRRADIATION

- **DOSAGE**
  - CHILDREN LESS THAN ONE YEAR - NO IRRADIATION
  - ONE TO TWO YEARS - 12 GY
  - MORE THAN 2 YEARS - 18 GY
  - ADULT ALL PROTOCOLS - 24 TO 30 Gy
CRANIAL IRRADIATION TECHNIQUE

• HIGH VOLTAGE CONDITIONS WITH TELECOBALT-60 MACHINE OR LINEAR ACCELERATOR-PHOTON ENERGIES MORE THAN 6 MV SHOULD NOT BE USED SO THAT THE BUILD UP REGION AT INITIAL DEPTH IS SUPERFICIAL TO THE MENINGES.

• DAILY SET UP-MASK TECHNIQUE

• IRRADIATION VOLUME-WHOLE NEUROCRANIUM WITH BOTH UPPER VERTEBRA (C2), THE RETROBULBAR TISSUE AND THE COMPLETE CRANIAL BASE WITH ITS MIDDLE CRANIAL GROOVE.
CRANIAL IRRADIATION TECHNIQUE

• EVERY FIELD SHOULD BE TREATED IN EVERY SESSIONS

• DAILY SINGLE DOSE IS 1.5 GY. THIS IS ADMINISTERED IN 5 SESSIONS PER WEEK UNTIL THE TOTAL DOSE HAS BEEN APPLIED

• ANGULATION OF THE BEAM (3-5 DEG POSTERIOR), HALF BEAM- TO AVOID OPTHALMOLOGICAL COMPLICATIONS
NEURAXIS IRRADIATION

• INDICATIONS-OVERT CNS LEUKEMIA IN ADULTS, ISOLATED CNS RELAPSE UNSUITABLE FOR CHEMOTHERAPY.

• DOSAGE- TO THE CRANIUM -24 TO 30 GY. TO THE SPINE-15 TO 18GY. 1.5 TO 1.8 GY /FRACTION.
NERURAXIS IRRADIATION

- FIELDS - LATERAL PARALLEL OPPOSED CRANIAL FIELDS, POSTERO-ANTERIOR SPINAL FIELDS

- COUCH AND GANTRY ROTATION - TO MATCH THE FIELDS

- MAXIMUM BEAM ENERGY 6 MV
TESTICULAR INVOLVEMENT

• INITIAL TESTICULAR INVOLVEMENT- RECENT OCCURRENCE OF A PAINLESS SWELLING OF THE TESTES WITHOUT SIGNS OF INFECTION, THEN A SONOGRAPHICAL EXAMINATION OF BOTH TESTES IS NECESSARY AND A BIOPSY IS NOT NECESSARY.

• IF UNCERTINITY EXISTS- ILLNESS INVOLVING INFECTION OR VASCULAR CHANGES OF THE TESTIS SHOULD BE RULED OUT AND A TESTIS BIOPSY SHOULD BE PERFORMED.
TESTICULAR INVOLVEMENT

• MANAGEMENT - IN THE CASE OF TESTICULAR INVOLVEMENT NO UNILATERAL OR BILATERAL ORCHIDECTOMY IS PLANNED.

• IF THE TESTICLE SIZE NORMALIZES COMPLETELY AFTER THE PROTOCOL AT THE LATEST ACCORDING TO TACTILE AND SONOGRAPHIC FINDINGS THERE IS NO EXTRA TESTICULAR IRRADIATION.

• IF AFTER THE PROTOCOL A DOUBTFUL CLINICAL FINDINGS REMAINS, BIOPSY IS REQUIRED AND IN CASE OF INVOLVEMENT LOCAL IRRADIATION MUST BE APPLIED.
TESTICULAR RELAPSE

• **TESTICULAR RELAPSE**-UNILATERAL OR BILATERAL PAINLESS BUT HARD SWELLING OF THE TESTIS (VOLUME >2) AND A BIOPSY SHOULD BE DONE.
• COMMON WITH T CELL ALL
• USUALLY FOLLOWS SYSTEMIC AND CNS RELAPSE
• POOR PROGNOSTIC FACTOR
• 1970-5%-15%
• WITH HD MTX-<2%
• **MANAGEMENT**: BOTH INTENSIVE SYSTEMIC THERAPY AND LOCAL RADIOTHERAPY
TESTICULAR IRRADIATION

• UNILATERAL IRRADIATION OR ORCHIDECTOMY AS LOCAL MANAGEMENT WAS FELT TO BE ASSOCIATED WITH A SIGNIFICANT RISK OF CONTRALATERAL DISEASE JUSTIFYING TREATMENT DIRECTED AT BOTH TESTIS FOR LEUKEMIA MANAGEMENT.

• 24 TO 30 GY OVER 2 TO 3 WKS (200CGY-300CGY/#)
TESTICULAR IRRADIATION

• TESTICULAR IRRADIATION IS ADMINISTERED VIA A SINGLE ANTERIOR PORTAL WITH THE USE OF ELECTRON BEAM OF APPROPRIATE ENERGY OR LOW ENERGY PHOTONS

• PATIENT IN A SUPINE POSITION AND THE PENILE SHAFT TAPPED UP AND OVER THE SYMPHYSIS PUBIS

• RECTANGULAR FIELD WITH MINIMUM OF 5 MM MARGIN TO THE SCORUM (INCLUDES BOTH TESTIS AND EPIDIDYMIS)
TESTICULAR IRRADIATION

• 10X10 CMS CONE PROVIDES ADEQUATE COVERAGE

• MOST APPROPRIATE ELECTRON ENERGY -9 TO 12 MEV

• A POLYSTERENE /LEAD BLOCK IS USED TO SUPPORT TESTIS AND SHIELD THE PERINEUM

• SKIN APPOSITION OF THE BEAM CAN BE ACHIEVED BY ANGLING THE GANTRY
TESTICULAR IRRADIATION

• IN THE ABSENCE OF ELECTRON BEAMS LOW ENERGY PHOTONS CAN BE USED (4 TO 6 MEV).

• TO ACHIEVE DOSE HOMOGENICITY .5 TO 1 CMS OF BOLUS OVER THE ENTIRE SCROTAL AREA MAY BE NECESSARY.

• SHIELDING OF THE UNDER LYING PERINEAL TISSUE IS PROBLAMATIC

• THE EXIT DOSE WILL BE HIGH.
MEDIASTINAL IRRADIATION

• IF A MEDIASTINAL TUMOR RECEDES <30% OF ITS ORIGINAL SIZE BY DAY 33 (MEASUREMENT CRITERIA – MAXIMAL DIAMETER TAKEN AT D5), THEN PHASE II OF THE SAME PROTOCOL IS TO BE CONTINUED.

• IF THE MEDIASTINAL TUMOR HAS NOT COMPLETELY RECEEDED BY DAY 33 (REMAINING TUMOR >30% OF ORIGINAL SIZE), THEN THE PATIENT IS PLACED IN THE HR BRANCH.

• IF ANY RESIDUAL TUMOR REMAINS IN THE CT /MRI AFTER A WEEK OF PROTOCOL THAT CAN BE RESECTED FOR HPE AND MOLECULAR GENETICS
MEDIASTINAL IRRADIATION

• IF NO VITAL INFILTRATES ARE FOUND CONTINUE IN THE SAME BRANCH. IF VITAL INFILTRATES ARE FOUND CONSIDER MEDIASTINAL IRRADIATION.

• DOSE-30-40 GY

• ALL T CELL PHENOTYPE WILL RECEIVE CONSOLIDATION RT.
TOTAL BODY IRRADIATION- BMT CONDITIONING

- TBI-CYTOTOXIC AND IMMUNOSUPPRESSIVE AGENT.

- ELIMINATE RESIDUAL LEUKEMIA AND EQUALLY EFFECTIVE IN MEDULLARY AND EXTRAMEDULLARY REGION.

- IT PERMITS ENGRAFTMENT OF DONOR IMMUNE AND HAEMATOPOIETIC CELLS. THE DONOR IMMUNE CELLS GENERATE THE GRAFT VERSUS LEUKEMIA EFFECT, AN IMPORTANT COMPONENT IN THE ERADICATION OF HOST LEUKEMIA.
TOTAL BODY IRRADIATION

• ALLOGENIC TRANSPLANT-ALL IN SECOND REMISSION AFTER AN EARLY RELAPSE, HIGH RISK ALL (PH +) AFTER FIRST REMISSION

• DOSE-200 CGY GIVEN IN BID WITH 6 HOUR INTER FRACTION INTERVAL 3 DAYS TO THE TOTAL DOSE OF 12 GY. DOSE RATE AVERAGE 8 TO 10 CGY PER MINUTE (MAXIMUM UP TO 15 CGY).
SEQULAE OF TREATMENT

- CNS IRRADIATION: (24 GY vs 18 GY VS MTX) SOMLONENCE SYNDROME, PITUITARY DYSFUNCTION, COGNITIVE FUNCTION DEFECTS, LEUKOENCEPHALOPATHY, SECONDARY MALIGNANCIES

- TESTICULAR IRRADIATION: STERILITY, LEYDIG CELL DYSFUNCTION (RARE).
SUMMARY

• ROLE OF RT IN ALL:

  • CRANIAL PROPHYLAXIS (MRG-T CELL ALL, HRG)

  • CRANIAL TREATMENT (ALL CNS INVOLVEMENT)

  • CRANIOSPINAL IRRADIATION (OVERT CNS INVOLVEMENT IN ADULT ALL, ISOLATED CNS RELAPSE)
SUMMARY

- TESTICULAR IRRADIATION (RESIDUAL, RELAPSE)

- MEDIASTINAL IRRADIATION (RESIDUAL, T CELL ALL, RELAPSE)

- TOTAL BODY IRRADIATION (SECOND REMISSION AFTER EARLY RELAPSE, HIGH RISK WITH FIRST REMISSION)