Not Too Old, Not Too Young - Cancer in the Adolescent and Young Adult

Hematology-Oncology Divisional Grand Rounds
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Topics to be covered
- Epidemiology & Etiology
- AYAs and Clinical Trials
- Unique psycho-social issues
- Late-effects
- Here in Buffalo...

“Children today are tyrants; they contradict their parents, gobble their food, and tyrannize their teachers.” Socrates

Epidemiology & etiology
- Each year, ~70,000 young adults and adolescents are diagnosed with cancer.
- 15-39 years old
- Lack of attention and progress in this age group

Children with cancer
- Advances among children with cancer have been dramatic
- Cooperative infrastructure
the facts

- Cancer is the #1 disease-related cause of death in AYA.
- Cancer develops 2.7 times more in the 15-29y age group than in <15y age group.
- Incidence of cancer has increased more rapidly in this group than in the younger population.
- Lack of improvement in survival rate compared to younger or older patients.

1971: US National Cancer Act

- Highly organized effort that has significantly improved the outcome of adults with cancer

Why is that?

- Disease?
  - differences in biology or tolerance of therapy

- System?
  - treatment by physicians less familiar with the disease
  - delay in recognition of malignancy
  - lack of available or failure to enroll pts on clinical trials
Psycho-social?
- unwillingness to participate in clinical trials
- delays in seeking medical attention with symptoms of cancer
- poor compliance with treatment

Shouldn’t someone do something about this?
- In 2006, NCI and Lance Armstrong Foundation published a report outlining recommendations to improve the outcomes of AYAs with cancer.

AYA and Clinical Trials
- Is there any benefit in enrolling?
  - Debatable
  - Impact on subsequent generations of patients
- Studies have indicated a survival advantage to children enrolled on clinical trials for ALL, NHL, Wilms tumor, and medulloblastoma.

> 90% of children <15y with cancer are treated at institutions that participate in NCI-sponsored clinical trials.

> 20% of 15-19y patients are seen at such institutions, and <10% enrolled in a clinical trial
  - Only 2% of 20-25y

Spares no geographic region or ethnic group.
What we have learned from clinical trials for AYA cancer

- Patients should be treated according to their disease, not their age.

Acute lymphoblastic leukemia

- >10y is a poor prognostic factor based on population-based analyses.
- Adolescent age group has lower incidence of favourable cytogenetic features, higher incidence of precursor T-cell immunophenotype and Philadelphia (Ph+) chromosome (though still much lower than adults).

ALL

- Retrospective analyses in the US, France and the Netherlands:
  - Pediatric regimens resulted in superior outcomes.
  - Nearly twice the event-free and overall survival rates.
  - Disease classification, presenting WBC, and cytogenetics were collected prospectively on treatment trials and were excluded for decreased survival.


- 15-20 yo
- 77 pts → FRALLE-93 (Pediatric)
  - High-risk
  - June 1993 – Nov 1999
- 100 pts → LALA-94 (Adult)
  - Std risk
  - Sept 1994 – May 2000
  - Retrospective analysis
  - Outcomes measured were CR (complete remission) and EFS (event-free survival)
Conclusion

- Similar clinical features in both groups
- Treated during the same period
- Low frequency of poor prognostic features

- Adolescents treated in the pediatric protocol had significantly better results for remission achievement and EFS


- CCG reported significant improvements in the outcome of high-risk pts, including adolescents (13-20y)
- CALGB also reported more favorable outcomes for younger adults in the last 10y with intensified post-remission therapy modeled after pediatric trials

- Determine whether the outcome for AYA pts differed between pediatric and adult group trials.

Differences in therapy

- CCG used risk-stratified therapeutic approach depending on marrow response at D7
  - Slow-early responders had received intensified post-remission chemotherapy
- CALGB uses 5-drug induction vs. 4-drug CCG
Conclusion

- Older adolescent and young adult patients with ALL had a significantly better outcome when treated on CCG vs. CALGB trials.
- CCG protocols had more vincristine, steroid, L-Asp, and significantly less cyclophosphamide and cytarabine.

Cure rates in Ewing tumor patients aged over 15 years are better in pediatric oncology units. Results of GPOH CESS/EICSS studies. Proc Am Soc Clin Oncol 22: 2003 (abstr 3279)

- Older age is poor prognostic factor in EWS.
- 1426 pts treated with standard therapy
- 73% were treated in ped onc units
- 10y EFS analyzed
  - Treatment in pediatric oncology units increases survival in all age groups.
  - Older age at diagnosis (> 15y) and treatment outside pediatric oncology units were significant risk factors.


- 190 pts > 18y.
- Pts who received therapy according to pediatric guidelines had similar outcomes to pediatric patients.
- Rate of response to chemo was similar to rate observed in children.
- Therefore, adults and children with RMS should receive similar treatment.
AYA Psycho-social Issues

- A cancer diagnosis and its treatment can impact every aspect of AYA development.

- Cancer is a huge challenge for AYAs:
  - Affects self-esteem – physical appearance, physical energy
  - Compromises education and work goals
  - Non-adherence issues

Psychological distress

- Compared to children, adolescents have more difficulty accepting a cancer diagnosis
  - 15-30% of childhood and young adult cancer survivors are seriously troubled psychologically and more likely to report distress
    - Adjustment difficulties
    - Delayed social maturation
    - Mood disturbances
    - Academic difficulties
    - Job and insurance discrimination
    - Relationship problems
    - Increased health concerns

Family and peer support

- Strong family and social support helps AYAs adapt to cancer
- Several studies identify family support and cohesiveness as a most important contributor to positive adjustment
  - However, some pts report emotional isolation from families and peers.
  - Parents expect to see them as strong, upbeat, pleasant
  - Sense of hopefulness and maintenance of self-esteem → “protecting mechanisms”

Support groups

- Support groups – good or bad?
- Reports on outings (such as picnics, adventure program, or family retreats) resulted in reports of improvements in self-confidence, independence, and social networking.

Non-adherence

- Adherence can affect survival.
  - Inadequate dosing linked to relapse and survival
  - Nonadherence to clinical trials can invalidate results and prevent adequate evaluation.

- Nonadherence among AYAs estimated to be 27-60%.
  - Positive family relationships and open communication between family members are positive factors that support adherence.
  - Overly controlling relationships (parents, health care professionals) have a negative impact on treatment adherence.

- Need for studies that look into effective strategies to promote adherence.

Where to treat them?

- Neither pediatric or adult wards are ideal:
  - Pediatric units – noise and crying, unsuitable activities, toys, books.
  - Adult units – less in common with elderly and dying patients.

- Ideally, Adolescent/Young Adult Units
  - 1990 – Teenage Cancer Unit (UK)
  - Medical staff specially trained to deal with social and psychological issues
  - Advantages are opportunities to share experiences with other pts, involvement of parents, age-related activities
When treatment ends…
- Challenges include transitioning from:
  - Diagnosis to long-term survivorship
  - Pediatric to adult medical care
  - Psychological and economic dependence to independence

AYA Cancer survivors
- Remember – 100% higher incidence of cancer in 15 – 19y vs. < 15y olds.
- Overall survival rate is >75%.
- Approximately 0.35% (1/286) of the population of adults > 30y will be survivors of cancer diagnosed between 15 – 29y of age.

Late effects
- Cancer therapy complications that persist or develops beyond 5 years from diagnosis.
  - Physical or psychological
- 2/3 will experience at least one late effect.
- ¼ severe or life-threatening late effect.

Late mortality
- Overall mortality 10-fold compared to general population.
- Risk of death significantly higher in females, cancer dx < 5y, initial dx of leukemia or brain tumor.
- Excess mortality was due to death from primary cancer, second cancer, cardiotoxicity and non-cancer death.
  - Up to 25y after the initial cancer diagnosis.

Here in Buffalo…
- Pediatric Hematology/Oncology Department
  - In-patient and out-patient services at WCHOB and RPCI.
- WCHOB:
  - Comprehensive Neuro-oncology Program
  - Pediatric Surgery, Pediatric ICU, Pediatric Subspecialties.
- RPCI:
  - America’s first cancer center founded in 1898 by Dr. Roswell Park.
  - Only upstate New York facility to hold the National Cancer Center designation of “comprehensive cancer center”
  - Member of the prestigious National Comprehensive Cancer Network.

AYA Oncology Program
- Multi-disciplinary approach
  - MD, Social Work, Psychology
- Assess each patient and identify psycho-social needs
- Fertility consult
  - Limited options for females for fertility preservation.
  - Sperm cryopreservation for males.
- Work with the treating department team
  - Educate pts about treatment trials
Patient database
- Future research
AYA Day
- Outing for our AYA patients during AYA week (1st wk of April).

Thank you!
- http://www.livestrong.org/What-We-Do/Our-Actions/Programs-Partnerships/LIVESTRONG-Young-Adult-Alliance