Assessing and Treating Depression and Anxiety in Children with Cancer

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HARVARD MEDICAL SCHOOL

Case 1

16 yo boy with no prior psychiatric hx in Consolidation II phase of treatment for High Risk ALL

Team requests consult for ? of depression

Past Hx: Baseline shy, quiet temperament, “Stone-faced but warm-hearted,” functioned well in school, had friends

No Family Psychiatric Hx

Initially coped well with treatment. CNS phase (last month) was more difficult with intense back pain, need to lie down, nausea. Current sx of anemia with shortness of breath and fatigue. Mood noted by team to be more sad and despondent.

Case 1 cont’d

Denies mood changes specific to steroids, although has significant withdrawal pain.

On interview, reports that he feels "bored" and that he very much misses school, and socializing with friends. He maintains contact with his friends on Facebook and denies that he feels depressed or sad in a consistent way. He feels that the worst part about being sick is the uncertainty about how he will feel physically. When he feels well, he reports that he likes to entertain himself on the computer or watching movies and feels better when able to do so.

Case 2

14 yo girl on longstanding therapy for multiply progressive cervicomedullary region low-grade astrocytoma.

Consult requested by mother and team for ? of depression.

On intermittent treatment since age 1year, complicated by growth hormone deficiency, hypothyroidism, partial adrenal insufficiency, early pubertal onset. Has hemiparesis and learning disabilities. Functions relatively well academically with IEP and individual supports.

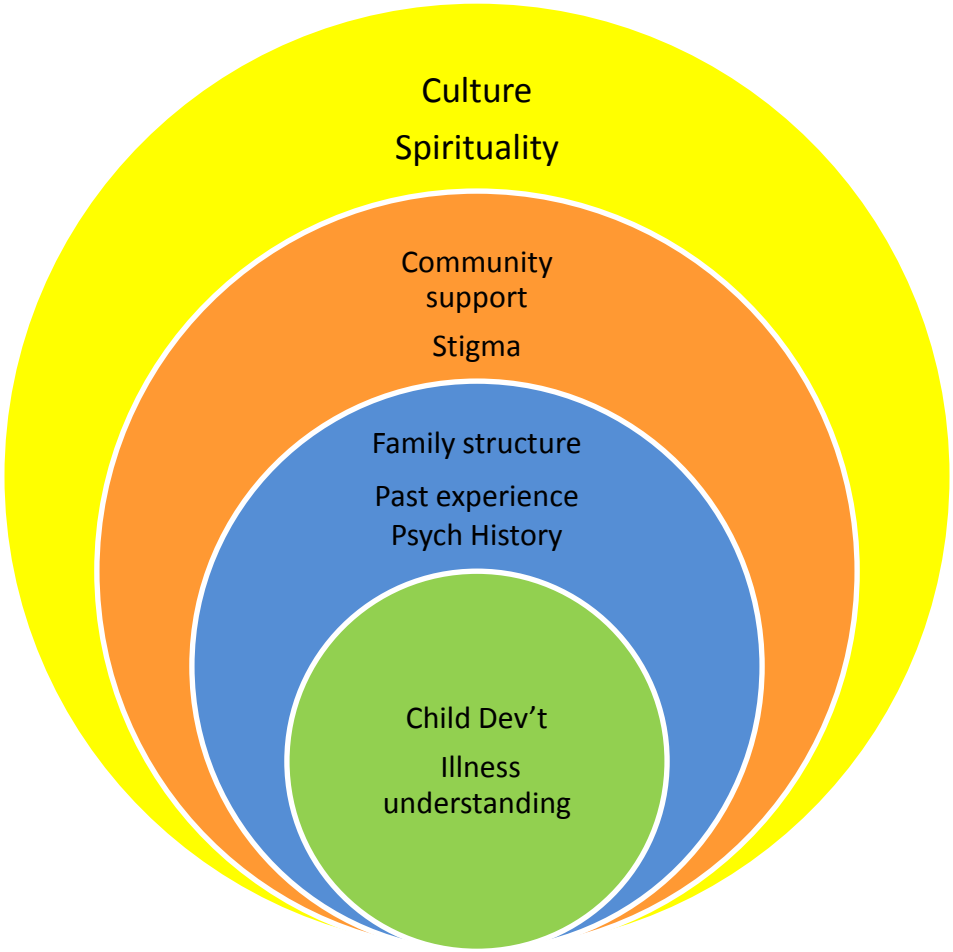
Family Hx includes depression in both parents, and alcoholism and bipolar disorder in the extended family.

Case 2 Cont’d

On low dose Ritalin to help with fatigue related to Temsirolimus.

Over the past year or so, she is more apathetic and irritable. She has had decreased interest in her usual activities: artwork, and going to the mall. She says that she "never knows what to do." She is also more aware of her peers and not being able to share in age-appropriate activities. She has thought about "stopping trying" to fight her brain tumor, but denies active suicidal ideation. She sleeps more and has low energy. Schoolwork is more difficult for her. She is generally eating well.

Child and Illness in Context



Consultation question:
Who is most distressed?

- Child's expression of distress
- Parental distress, grief, depression
- Medical caregiver distress, grief, helplessness
- Over/ underestimation of suffering by parents/ medical providers

Identifying strengths and supports

- Who… is in the family, what roles do they play?
- What…are sources of meaning making, support?
- Where…is this family at their best?
- When…in the disease trajectory are they?

History gathering

- Child's pre-existing:
  - Development
  - Temperament
  - Coping style
  - Psychiatric history

- Family Psychiatric History
  - Depression/ Bipolar
  - Anxiety
  - Substance abuse

Differential Diagnoses
Change in mental status/ mood/ anxiety

- Rule-out "Organic" syndromes
  - Delirium
  - Catatonia
  - Medication induced mood/ mental status changes
  - Pain
  - Nausea, malaise, fatigue
  - Primary CNS lesion
  - Seizure

Prevalence

	General Population	Medically Ill Children	Acute Lymphoblastic Leukemia 2-10 yo
Major Depression	School age: 2% Adolescent: 4-8%	7-32% Kersun, 2007	5-7%
Anxiety	13% Mean onset 11yrs Emslie, 2004	7-40% Pao, 2010	11% ->4% Myers, 2014

Depression
Differential Diagnosis

- Adjustment disorder with depressed mood
- Sadness, grief
- Behavioral regression
- Anxiety
- Parental perception/ concern
- Staff perception/ concern

- Dysthymia – subacute, > 1 year
- Bipolar Disorder

Major Depressive Disorder

DSM 5

At least one of:

- ***Depressed mood: sad, empty, "bored," "blah," irritable***
- ***Loss of pleasure, Anhedonia, no interest in all/almost all activities***

≥5 symptoms/ changes in:

Sleep: insomnia/ hypersomnia
Interest: decreased
Guilt: worthless, hopeless
Energy: fatigue
Concentration: decreased
Appetite: decreased/ increased
Psychomotor agitation/ retardation
Suicidal ideation: passive v active

- **Cause significant distress or impairment ≥ 2 weeks**

Suicidal Ideation

Assess:

- History of suicide attempt in child, family or peers
- Passive v active ideation
- Ideas about afterlife, survivors
- Plan
- Intent

- Request for hastening death

Case 3

Danny is an 11 yo boy with newly diagnosed ALL. He has a history of being “high-strung” and being a “worrier,” but has not needed any psychological intervention to date. His father has a history of OCD and anxiety.

During outpatient consolidation II therapy he becomes more fearful about his health, with increased anticipatory nausea, and stalling around port access.

As he resumes school, he is extremely worried about keeping up with school and cannot accept accommodations from teachers. He needs to repetitively talk through his worries for long periods at night with his mother and has trouble falling asleep.

Anxiety Disorder

Differential Diagnosis

- Physical symptoms: pain, dyspnea
- Procedural/ anticipatory anxiety
- Separation anxiety
- Medical trauma/ terror/ PTSD
- Parental/ staff anxiety
- Uncertainty/ misconceptions/ fears about illness
- Lack of communication/ secrets

Consider pre-morbid temperament and family history

Treatment of Depression/ Anxiety

Non-pharmacologic

- Cognitive Behavior Therapy/ Behavioral medicine
  - Psychoeducation of child and parents
  - Reframing depressive/anxious cognitions
  - Distraction, behavioral activation
  - Relaxation training/ biofeedback/ hypnosis
  - Effective for coping with pain, nausea
- Emotional-expressive psychotherapy/ play therapy
- Family Intervention
- Child life involvement

Psychopharmacology

- Whose distress are you treating?
- What is the parent/ child's attitude towards psychotropic medication?
- Drug-drug interactions
- Who will prescribe?
- How will you know that medication is working?

Serotonin Specific Reuptake Inhibitors

For Depression, Anxiety, OCD

- Well-tolerated, side effects mild and attenuate over time
- Maximum effect at 4-6 weeks, up to 8-12 weeks
- Extremely limited data in medically ill children

Cautions:

- 2003 FDA black box warning re: increased incidence of suicidal ideation 2% placebo v 4% on SSRI with no completed suicides
- 2004: “close monitoring for worsening depression or SI”
- Activation, mania

Interactions:

- Linazolid - MAOI-B
- Lovenox – platelet aggregation

SSRI use in children with cancer

- 50% pedi oncologists at CHOP prescribe SSRI's for sadness, anxiety and depression

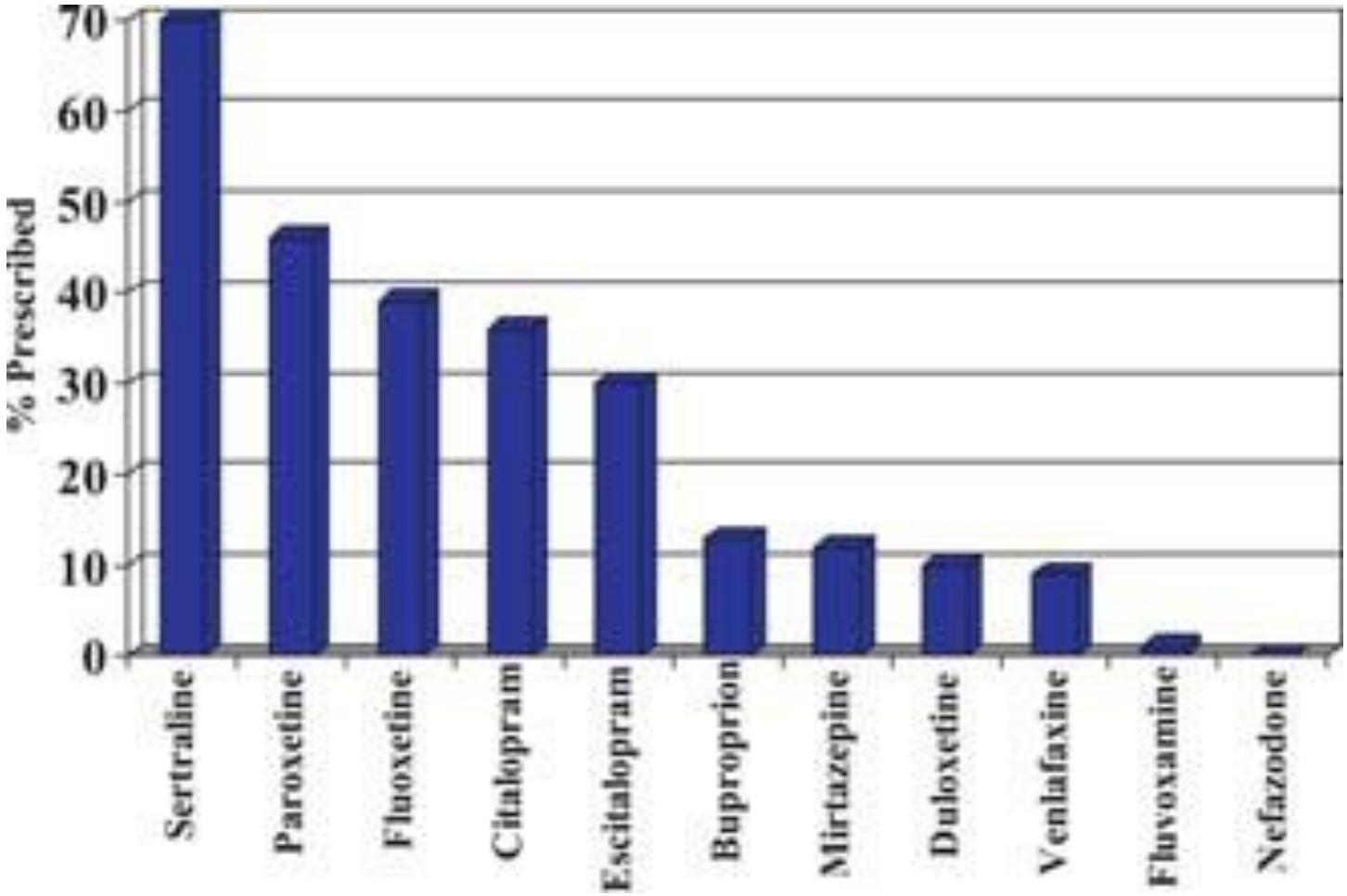
  40% < 6 mos, 40% 6-12 mos, 20% >12 mos Kersun & Kazak, 2006

- 10% patients at CMC of Dallas received antidepressants within 1 yr of dx

  Highest rates among adolescents, ALL pts, and those receiving opiate analgesia and radiation Portteus, 2006

- 7 % of patients admitted to pedi onc NCI study center received antidepressants Pao, 2006

Pediatric oncologists' practices of prescribing selective serotonin reuptake inhibitors (SSRIs) for children and adolescents with cancer: A multi-site study



Pediatric Blood & Cancer
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http://onlinelibrary.wiley.com/doi/10.1002/pbc.22788/full#fig2

SSRI studies in children with cancer

Fluvoxamine n=15, tolerated well

- 64% with MDD had 50% decrease in reported sx at 8wks
- 80% with anxiety had 50% decrease

Gothelf D, 2005

Citalopram n= 4, study d/c'd due to FDA warning

- No side effects
- Significant improvement in 2 weeks -> 12 wks

DeJong, 2007

Serotonin Specific Reuptake Inhibitors

	Dose range	FDA approval	Considerations
Fluoxetine	10-80mg	• >5 yrs sel mutism • > 7 yrs OCD • > 8 yrs depression	Up to 16 day half life
Sertraline	25-200mg	> 6 yrs OCD, depression	GI SE?
Citalopram	10-40mg	none	? QTc prolongation at higher doses
Escitalopram	5-20mg	> 12 yo	Low SE
Paroxetine	10-40mg	none	Short-half life and withdrawal sx

SSRI Drug Interactions

Table 1

Inhibitory Effect of SSRIs on CYP-450 Isoenzymes

	CYP-450 Isoenzymes				
Agent	**CYP-1A2**	**CYP-2C9**	**CYP-2C19**	**CYP-2D6**	**CYP-3A4**
Citalopram	0	0	0	+	0
Fluoxetine	+	++	+/++	+++	+/++
Fluvoxamine	+++	++	+++	+	++
Mirtazapine	0	0	0	+	0
Nefazodone	0	0	0	+	+++
Paroxetine	+	+	+	+++	+
Sertraline	+	+	+	+/++	+
Venlafaxine	0	0	0	+	+

SSRI: selective serotonin reuptake inhibitor; CYP: cytochrome P; 0: minimal/no inhibition; +: mild inhibition; ++: moderate inhibition; +++: potent inhibition.

Source: References 12, 13, 14.

Brown CH. *US Pharm.* 2008;33(1):HS-3-HS-19

Serotonin Syndrome

- Rare side effect
- Usually associated with multiple serotonergic agents
- Hyperthermia, hypertension, diaphoresis, shivering, tremor, myoclonus, seizures, ataxia, delirium, restlessness

- Supportive management
- Methysergide and cyproheptadine may be useful adjuncts

Stimulants

Methylphenidate

For Depression, Fatigue, Apathy

- Immediate effect
- Titrate to effect, may convert from short to longer acting

Cautions

- Associated with serious cardiovascular events in patients with pre-existing structural cardiac abnormalities cardiomyopathy, arrythmias
- Monitor side effects of increased anxiety, agitation, anorexia, psychosis

Benzodiazepines

For Anxiety, Agitation (without confusion)

- Short acting - Lorazepam
  - procedures
  - sleep initiation
- Longer acting - Clonazepam
  - lasts 6-8 hrs, ½ life 22 hrs
  - double potency

Caution:

- Sedation, paradoxical reactions, worsening delirium

Discussion

- Challenges in assessment
- Therapeutic decision-making
- Challenges to implementation
- Assessing efficacy