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Advanced Pediatric Psychopharmacology

Postraumatic Stress Disorder and Reactive Attachment Disorder: Outcome in An Adolescent

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Chief Complaint and Presenting Problem

T., A 12-YEAR-OLD Hispanic boy, was transferred to a state children's psychiatric hospital for management of "behavioral problems." He admitted to getting angry and breaking things and complained of insomnia, nightmares, and frequent nervousness.

History of Present Illness

T. was reported to have a long history of aggressive, assaultive, and unpredictable behavior, angry and irritable moods, impulsivity, hyperactivity, enuresis, and a history of nightmares and flashbacks. T. had experienced four prior psychiatric hospitalizations. Prior to the current transfer, during an approximately three-month stay at a private hospital, T. was reported to have become increasingly aggressive, assaultive, and impulsive, requiring frequent as-needed medications including intramuscular injections of lorazepam, haloperidol, and chlorpromazine. Lorazepam and other benzodiazepines were thought to cause disinhibition and worsened his behaviors. Upon transfer to the state children's psychiatric hospital, T. carried diagnoses of mixed bipolar disorder, thyroid abnormalities, asthma, and possible fetal alcohol syndrome.

Upon transfer, T.'s medications included risperidone 3 mg, clozapine 200 mg, valproic acid 750 mg, guanfacine 4 mg, and desmopressin 0.6 mg. His as-needed medications were chlorpromazine 50 mg every two hours, with a maximum of four doses daily, Benadryl 50 mg every four hours, and albuterol inhaler two puffs every four hours with a maximum of four doses daily. The clozapine dose had been adjusted downward in the previous hospital due to sedation and drooling.

Past Psychiatric History

T. had been hospitalized four times, at ages 6, 7, 8 and 12; each lasted 1–3 months. The last hospitalization led to transfer to the current state hospital. From age 7 to the present,

T. lived primarily in foster care or at a residential treatment center when he was not in the hospital. Prior diagnoses given on discharge summaries included intermittent explosive disorder, oppositional defiant disorder, rule-out bipolar mood disorder not otherwise specified (NOS), and rule-out conduct disorder. It was noted that hospitalizations were usually triggered when foster or group home parents went on vacation or when T. had a rare visitation with his biological mother.

T. was first hospitalized at age 6 for increasing aggression and reportedly smearing feces and fondling his younger sibling. He was also noted to have no friends and to frequently threaten to kill himself when limits were set. There were also sexualized behaviors towards his younger stepbrothers; his father and stepmother described him as "never happy," stealing food and money, lying when caught, and hoarding food. He was also fascinated by guns and violence. All of the above led to suspicion of neglect and physical and/or sexual abuse of T. at an earlier age. T.'s parents requested out of home placement for him at age 7 for many reasons, including fear for the safety of the other children, and he was placed in therapeutic foster care.

T.'s second hospitalization occurred at age 7 due to an increase in aggressive behavior. He also reported experiencing command auditory hallucinations telling him to hurt people. His thinking was disorganized, characterized by strained reasoning, poor judgment, and suspicion. It was noted that he often misinterpreted his environment and his interaction with others, and preferred to isolate himself from his peers. After about two weeks of medication adjustments, therapeutic milieu, and individual therapy, he began to show improvement in his ability to resist assaulting others. His diagnosis at discharge was psychotic disorder, NOS.

The third hospitalization occurred at age 8, also for acting out and aggressive behavior, although the treatment records were unavailable from this hospitalization. He was apparently discharged to a residential treatment center at the end of this hospitalization.

Developmental History, Including Pregnancy, Birth, Infancy

There was some suspicion that the biological mother may have used marijuana, alcohol, and perhaps cocaine during pregnancy, which the biological mother denied. The patient was born by Caesarean section. There was no information available on developmental milestones. Records indicated that the baby bonded/attached to his mother, and that when he was crying and in distress she would pick him up and he would respond to her touch and comfort.

The parents divorced when T. was less than 1 year old, and his mother received custody; however after one year, she decided that she could not care for him any longer. The mother reportedly had ongoing drug abuse during this time involving cocaine and marijuana. While living with his mother, T. was sent from one baby sitter to another and also sometimes lived with his mother's friends until the biological father regained custody when T. was $2^1/_2$ years old. His father remarried; at age 5–6, T. was living with his father (age 26) and stepmother (age 24), one stepsister and four stepbrothers, ranging in age from 2 to 8.

Educational History

T. has been in special education classes since kindergarten. He repeated third and fourth grades for behavioral problems. He was noted to have "difficulty in learning" and was "exhibiting sexually inappropriate behavior in school." He reportedly struggled with peer relations at school. Prior to the most recent hospitalization, T. had been in the fifth grade in a special education setting, with a 1:1 paraprofessional.

Social History

T. was allegedly sexually abused by the biological mother, although the full details of this were never disclosed. There were also reports of physical abuse by his biological father, and T. reported flashbacks of "being beaten" by the father. However, there are conflicting reports from different family members about the biological mother, biological father, and stepmother. There was one report that T. may have been hit in the head by the stepmother and had food withheld for punishment.

There were conflicting reports by his grandmother and others regarding T.'s ability to initiate and maintain friendships. T. enjoys playing with action figures, bike riding, roller-skating, skate boarding, and drawing. He likes to play basketball, hunt with his grandfather, and make bows and arrows out of wood.

Currently, his biological mother has only supervised visitation, which takes place sporadically. T. is reported to have little contact with his biological father and stepmother.

Family History

Records report that the patient's biological mother has depression and bipolar illness. She was also reported to be addicted to cocaine and marijuana. The biological father had attended a special educational setting as a child for attention-deficit/hyperactivity disorder (ADHD) and behavioral difficulties. The biological father had also been reportedly addicted to marijuana. He is currently incarcerated, and a

half-brother is also in jail, allegedly for conviction in a sexually related crime.

Previous Psychological Testing

Psychological evaluation was conducted when the patient was 6 years old. The summary indicated "at least low-average intelligence." The patient displayed an uneven pattern of functioning across attentional measures but appeared to have marked difficulty on those that required sustained attention or inhibiting impulsive responding. These tests also highlighted clinically severe fine motor control problems, attentional problems, and difficulties with disinhibition, suggesting ADHD, primarily hyperactive-impulsive type, which may be comorbid with a mood disorder.

Psychological testing was repeated prior to transfer, but this was when T. was sedated and on substantial doses of medication, including risperidone, clozapine, valproic acid, guanfacine and desmopressin. The results on the Weschsler Intelligence Scale for Children, Fourth Edition (WISC-IV) included a full scale IQ of 65, with subscale scores of verbal comprehension 65, perceptual reasoning 82, working memory 72, and processing speed 62. There was a great deal of scatter noted on subtests.

During this admission, T. was screened for ADHD with Swanson, Nolan and Pelham (SNAP) rating scales, and met the 95% cutoff criteria for ADHD and oppositional defiant disorder.

Medical History

T. has a history of possible exposure to cocaine and alcohol *in utero*. There is some question of mild fetal alcohol syndrome manifest by mild facial dysmorphia noted in previous records. There was a history of thyroid problems, details unknown, in the past. He also has mild asthma.

Medication History

Past medications include risperidone, paroxetine, perphenazine, loxapine, haloperidol, olanzapine, quetiapine, aripiprazole, valproic acid, propranolol, and bupropion, but the dosages and time frames used are not available. It is known that he was discharged from his second hospitalization at age 7 on quetiapine 600 mg, perphenazine 24 m., and valproic acid 750 mg daily.

Mental Status Examination on Admission

T. is a Hispanic pubertal boy appearing his stated age wearing a T-shirt and shorts, with flip-flop sandals. There were not any readily apparent facial dysmorphias. His speech was mildly slurred but understandable. He was notably sedated, drooling at times. His mood was described as "ok," but his affect appeared constricted in the dysphoric and irritable range. He was noted to be hypervigilant and to become quite irritable very quickly, yelling "Don't touch me! Don't touch me!" whenever he perceived someone approaching toward him. He denied suicidal or homicidal ideation, and he further denied any perceptual distortions, including auditory or visual hallucinations. His thought processes were disorganized, and there was a paucity of thought content. His insight and judgment were deemed poor. On

admission, he was noted to be oriented to name, place, and time, but no other cognitive testing was done at that time.

Hospital Course

Upon admission, T. displayed mood instability, poor judgment, and verbal and physical threats to harm peers and staff. He was extremely assaultive and aggressive. He was unable to use words to express his feelings, which resulted in him spitting, biting, kicking, cursing, and hitting during times of crisis. He was placed on constant observation (1:1) upon admission due to the severity of his aggression. He reported occasional nightmares, was described as hypervigilant around all staff, and occasionally had early insomnia.

Medical workup, including physical exam, blood chemistries, neurological examination, and an MRI of the spine were within normal limits.

T. remained aggressive in the hospital for many months (Fig. 1). His treatment consisted of behavioral and pharmacologic intervention used in combination. Over the final five months of hospitalization, the patient showed remarkable improvements, with less overall number of incidents and with less violence in each episode (Fig. 1).

There was never a time during this greater \sim 8-month hospitalization in which there was any evidence of a bipolar or any psychotic disorder. During his time in the hospital, the patient did not display sexually inappropriate or fire-setting behaviors.

Pharmacological Management

After admission, T. was gradually tapered off of risperidone 3 mg, clozapine 200 mg, and valproic acid 750 mg. A trial of lithium was started but discontinued after anger and behavioral problems notably increased. He was initially given chlorpromazine only on an as-needed basis, with doses

ranging from 25–100 mg by mouth (PO) or intramuscular (IM), usually given once or twice per week. Other medications included diphenhydramine 100 mg PO or 25 mg IM and risperidone M tabs 1 mg PO as needed. These were given also 1–2 times per week during the first several months. Standing doses of chlorpromazine were added, initially 25 mg three times daily (tid) and increased to 50 mg four times daily, which caused substantial sedation. Later, chlorpromazine was lowered, and sertraline was begun to target the aggression (Siegel et al. 2007). Sertraline was titrated up slowly to a total dose of 125 mg daily.

Notably, despite a childhood diagnosis of ADHD, T. had never had a trial of stimulants, as far as could be determined from available records and from grandparents. A trial of immediate-release methylphenidate was started and titrated up to 15 mg PO tid with no adverse effects. There was a dramatic improvement in his attention, concentration, and hyperactivity. Guanfacine (titrated up to a total dose of 2 mg daily) was added to address residual impulsivity and irritability, which also was beneficial in controlling this behavior. Towards the end of T.'s hospital course, in order to simplify his medication regimen, the immediate release methylphenidate was changed to extended release Concerta 54 mg daily, which he also tolerated well.

During tapering of the chlorpromazine, T. was noted to have some pill-rolling, shoulder shrugging, and stiff gait, which was felt to be due to withdrawal dyskinesia. Given the extrapyramidal symptoms and emergence of a possible withdrawal dyskinesia, it was decided to slow the taper of chlorpromazine, and he was discharged on a very small dose of chlorpromazine. Desmopressin was given for enuresis with resolution of symptoms.

During the hospitalization, T.'s height increased from five feet two inches to five feet four and one half inches, and his weight increased slightly from 134.5 lbs to 137 lbs.

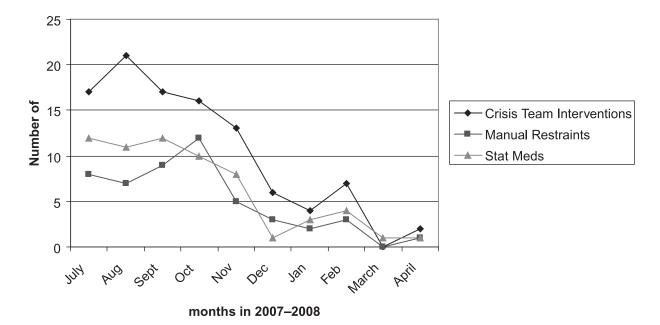


FIG. 1. Number of incidents including crisis team interventions (calls overhead for assistance), manual restraints, and urgent medications (by mouth or intramuscular) for each month during the course of this patient's hospitalization.

Psychosocial Treatment

Family work included T.'s paternal grandparents and his biological mother. In the beginning, all members attended and participated in sessions, although not as often as optimal due to transportation constraints, but eventually the mother stopped attending family meetings. In individual sessions, T. eventually was able to utilize verbal, play, and pet therapy modalities as well as some elements of CBT; self-control strategies including taking time out, verbalizing his feelings, counting, and deep breathing all worked well for him. As he progressed, the patient was able to be a more active and appropriate participant in group therapy sessions.

Overall, T. made significant progress from the time of admission until discharge more than eight months later. T. was discharged to the care of his paternal grandparents and outpatient follow-up.

Brief Formulation

In summary, T. is a 12-year-old Hispanic boy with a child-hood history characterized by neglect and abuse, and a history in the past six years of repeated hospitalizations, institutionalization, and/or placement with foster families. Primary symptoms include hypervigilance, nightmares, and impulsive, hyperactive and aggressive behavior.

Biologically, there is a family history of ADHD and incarceration on the paternal pedigree. There is also a prominent history of drug use by the biological parents, including alcohol, marijuana, and cocaine, and putative *in utero* exposure to these substances resulting in mild dysmorphia noted by some health care workers, possibly consistent with fetal alcohol syndrome. Psychologically, this child never had a secure attachment figure, and was ultimately hospitalized and now institutionalized. Socially, the patient has had very little support from family members and very few meaningful object relations. On the side of strengths, the paternal grandparents are available and seem to genuinely care for this child, although they can easily become overwhelmed when he becomes aggressive.

Multi-Axial Diagnoses

Axis I: Post traumatic stress disorder (PTSD) Reactive attachment disorder (RAD) ADHD

Rule-out oppositional defiant disorder (ODD)

Axis II: Expressive language disorder Learning disorder NOS Rule-out mild mental retardation

Axis III: History of thyroid abnormalities Exposure to cocaine and alcohol *in utero*; possible mild fetal alcohol syndrome

Axis IV: Conflicted relationship with peers at residential treatment facility; history of residential placement and psychiatric hospitalizations.

Axis V: GAF: 35-45.

Discharge Medications

Guanfacine 2 mg twice daily (bid) Sertraline 125 mg in the morning (AM) Chlorpromazine 75 mg AM Concerta 54 mg AM

Discussion

T. is an adolescent who illustrates the complexity of outcomes in a child with extreme early adversity who experienced likely prenatal exposure to alcohol, marijuana, and cocaine followed by abuse and neglect in the first few years of life. His childhood was characterized by loss of primary objects, multiple placements, and hospitalizations. Diagnostically, the patient appears to have met criteria for RAD, ADHD, and PTSD (Bowlby, 1982). Once adequately treated with a stimulant for his ADHD, the symptoms of aggression and defiance markedly decreased, although it is still possible that T. meets criteria for ODD. There was never any real evidence for bipolar or psychotic disorders, although these diagnoses had been given in the past without clear documentation of symptoms.

The essential feature of RAD is markedly disturbed and developmentally inappropriate social relatedness in most contexts that begins before age 5 and is associated with grossly pathological care. There are two types of presentations. In the inhibited type, the child persistently fails to initiate and to respond to most social interactions in a developmentally appropriate way. The child shows a pattern of excessively inhibited, hypervigilant, or highly ambivalent responses, including frozen watchfulness, resistance to comfort, or a mixture of approach and avoidance. The other type of presentation is the disinhibited type, in which there is a pattern of diffuse attachments. The child exhibits indiscriminate sociability or a lack of selectivity in the choice of attachment figures. The disturbance is not accounted for solely by developmental delay (e.g. as in mental retardation) and does not meet criteria for pervasive developmental disorder (DSM-IV-TR).

T. appears to meet criteria for the inhibited type, as he was not overly familiar with or seeking comfort from unfamiliar adults. He was impulsive in terms of ADHD symptomatology, but not in a socially disinhibited way. This inhibited phenotype is also to be distinguished from social phobia; T. was hypervigilant and aloof even with familiar caregivers, rather than only in social settings. The RAD likely interfered with his capacity to initiate and maintain friendships, but to further add to the complexity of differential diagnosis, must also be distinguished from the social deficits which are core feature of pervasive developmental disorders.

Another challenge in differential diagnosis is the question of whether T. also meets criteria for PTSD, since there is overlap with RAD symptoms. Certainly the hypervigilance, insomnia, and nightmares are consistent with PTSD. In addition, hyperarousal can also render children who have been traumatized more vulnerable to having difficulty in the regulation of aggression, leading to oppositionality and explosive defiance (Donnelly, 2003). Not surprisingly, there is recent evidence that children with disinhibited attachment disorders are more likely to develop PTSD in response to traumatic events, including physical and/or sexual abuse (MacDonald et al., 2008).

There has been very little investigation of the long-term course and outcome of RAD; most of the database on these youth derive from four longitudinal studies of children raised in institutions (AACAP Practice Parameters, 2005). These studies indicate that persistence of inhibited RAD symptoms is rare in children adopted into more nurturing

environments (AACAP Practical Parameters, 2005). A minority of these adopted, institutionalized youth continue to exhibit deficits in peer relations (Hodges and Tizard, 1989). Some studies have documented that children from early environments in which abuse and neglect have occurred may also have both RAD and PTSD symptoms (Hinshaw-Fuselier, et al 1999). However, systematic study of comorbidity between PTSD and RAD is lacking (Cicchetti et al 1995).

No psychopharmacological controlled trials for RAD have been conducted. However, given the overlap of symptoms of maladaptive emotion regulation, hypervigilance and social withdrawal, pharmacological treatment for the comorbid PTSD, ADHD, and disruptive behavior disorders is often indicated in children who are diagnosed with RAD (AACAP Practice Parameters, 2005).

The evidence base for efficacy of pharmacological treatments for PTSD in youth is limited, in contrast to the adult literature (Donnelly, 2003). Although sertraline and paroxetine have been FDA approved for treatment of PTSD in adults, there are no specific medications approved for children and adolescents. There is only one controlled study of medication in such youth. Cohen and colleagues reported in a study of 24 youth, ages 10–17, with PTSD, that sertraline added to trauma-focused CBT provided no clear benefit over trauma-focused CBT plus placebo (Cohen et al. 2007). The authors concluded that there was only minimal evidence of added benefit of medication, supporting an initial trial of trauma-focused CBT or other evidence supported therapy in children with PTSD (Cohen et al. 2007). Most major drug categories have been studied in uncontrolled designs, including other serotonergic agents, alpha adrenergic agonists, atypical neuroleptics, beta adrenergic antagonists, benzodiazepines, mood stabilizing anticonvulsants, lithium, and opioid antagonists (Donnelly 2003). Pharmacologic intervention should be considered when target symptoms such as agitation, aggression, insomnia, mood difficulties, or anxiety cause distress or interference to the child. Medication should always be used in combination with psychosocial intervention including psychoeducation, individual and family therapy and cognitive behavioral approaches (Donnelly 2003).

Fortunately, T. responded well to his treatment over time during the most recent hospitalization, which combined pharmacological interventions with behaviorally oriented psychosocial interventions. There is no doubt that the role of the milieu itself was significant, in that T. benefited from stable, consistent, firm but warm interventions of staff. With regard to the pharmacotherapy, it is notable that this child had been treated with atypical antipsychotics, including clozapine, for unclear and off-label indications; chlorpromazine, used initially as an as needed treatment for aggression, was able to be reduced to a modest level and given as a standing dose. It appeared that the extrapyramidal symptoms, including the withdrawal dyskinesia, resolved during the hospitalization. It is unfortunate, given T.'s diagnosis of ADHD as a young child, that he was not given a trial of stimulant or other medication for ADHD in the past. One of the important interventions of the recent hospitalization was the addition of a stimulant to which T. responded dramatically.

The prognosis in T.'s case is to be determined. Given that he is at risk for guarded long term outcome as a result of his disrupted early attachments, abuse and neglect, disruptive behavior disorder and family history of ADHD, substance abuse and mood disorder, close follow-up and ongoing intervention is essential.

Disclosures

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