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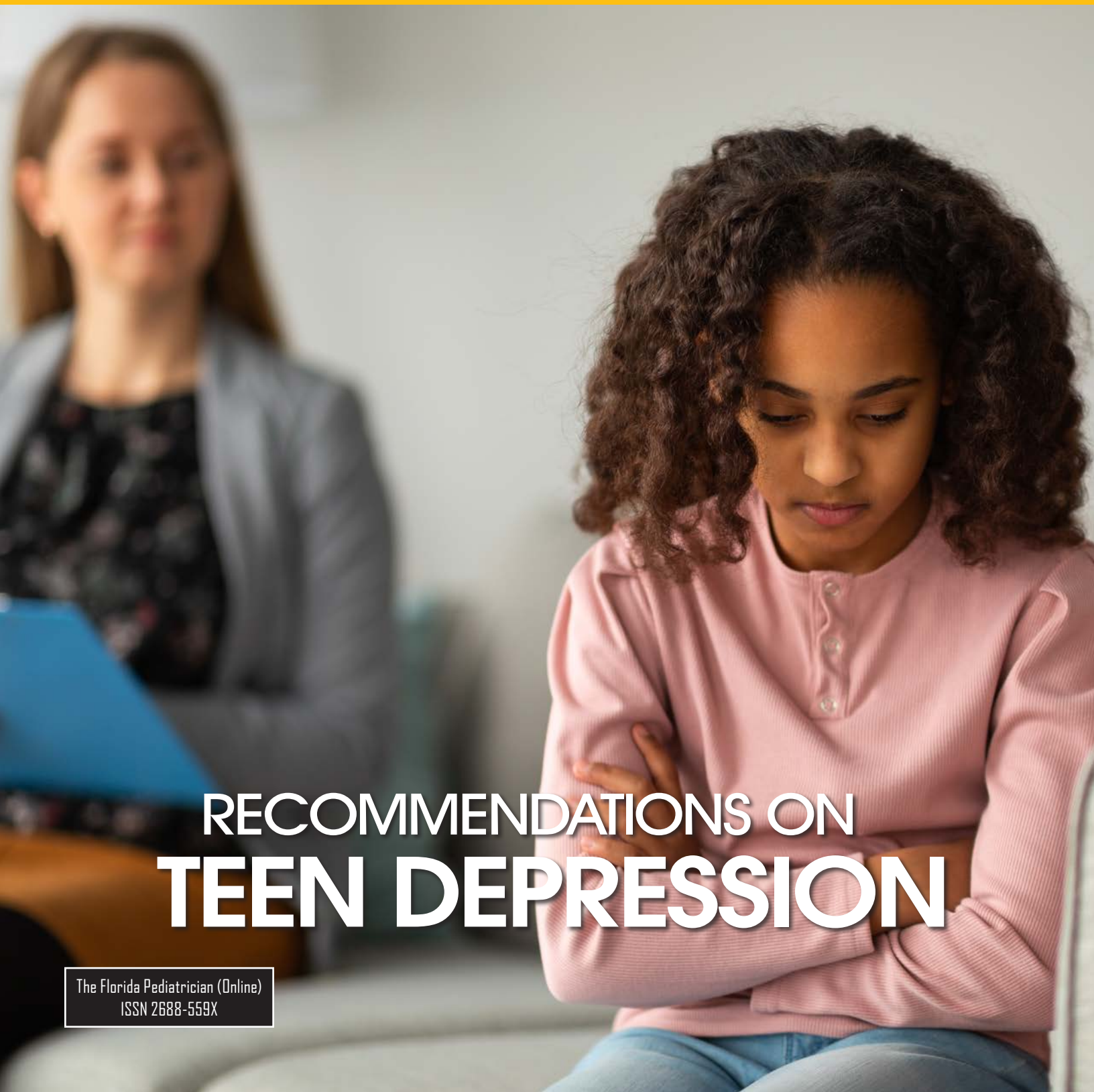

RECOMMENDATIONS ON TEEN DEPRESSION

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Resident Match Day!

Pediatrics had another successful match.

Congratulations to all who matched in pediatrics and welcome to the most rewarding specialty in all of medicine. You, like the rest of us, obviously did not choose pediatrics for financial reasons. You chose it because you want to do good in the world. You want to help children and families. You are a class by yourself. What you will do in your practice will change the lives of children and families. Not only you will be providing healthcare, but you will bring good health to children. You will be advocates for children and families.

You will have good days and you will have bad days. As long as you focus on the greater good you will have a fulfilling career. Think of pediatrics as more than a profession. Make it your passion, and you will never go to work again. That is how I feel 40 years later. You will achieve tremendous rewards and face many frustrations; every line of work has that. I will guarantee that the rewards are greater than the frustrations and that will keep you going.

Residency is what you make of it. You will learn more during residency than anytime in your professional career. Make the best use of it and enjoy your training. Create memories and make friendships. Yes, there will be many like me who will tell you that you have it easy compared to "when we were residents," and that is not necessarily a bad thing. To borrow from JFK "Ask not what the residency program can do for you to teach you. Ask what you can learn in your residency." How much or how little you learn at the end of the day is going to be your gain or your loss.

Pediatricians are unique because we are not only interested in advocating for ourselves; we are also committed to advocating for children and families. Even the name of our professional organization, the Florida Chapter of the American Academy of Pediatrics (FCAAP) instead of the Florida Chapter of the American Academy of *Pediatricians*, reflects our commitment to children and families.

To be successful in your advocacy for pediatricians, children, and families, you need a village, and your village is FCAAP. Not only should you become a member of FCAAP, but you should become an active participant. Ask your program directors about FCAAP and how you can become active in FCAAP. You can also reach out to admin@FCAAP.org and let the FCAAP know that you want to be active with the chapter. It is your chapter, and you are the future of it.

Lastly, find a mentor who can help and guide you and will be your advocate and advisor throughout your career.

Best of luck!

Mobeen H. Rathore, MD, CPE, FAAP, FPIDS, FSHEA, FIDSA, FACPE
Editor, The Florida Pediatrician

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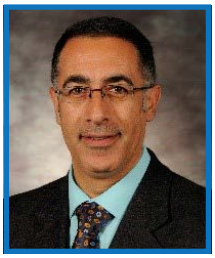

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REVIEW ARTICLE

Recommendations on Teen Depression for the Primary Care Provider

Jasmine M Reese, MD MPH FAAP FSAHM
Johns Hopkins School of Medicine, Johns Hopkins All Children's Hospital

"I thought my pediatrician was the wrong person to talk to about my depression". This is a statement made by a 14-year-old adolescent that was seeking help from her pediatrician regarding changes in her mood and was discharged from clinic before any discussion or evaluation took place. It is "old thinking" to say that when a pediatric patient has concerns about feeling depressed that they should only be seen by a psychiatrist or a psychologist. The unfortunate reality is that many teens are struggling with mood changes, including depression. Pediatricians are the front-line providers to help them navigate first steps in screening, diagnosis, and initial management.

According to the National Institute of Mental Health, approximately 4.1 million adolescents ages 12-17 years had at least one episode of major depression. The prevalence of Major Depressive Disorder (MDD) in children and adolescents is approximately 2% and 13%, respectively. Adolescent females tend to have higher rates of depression when compared to males.[5] The lifetime prevalence is 20% by age 20 years old.[17] According to the National Youth Risk Behavior Survey there has been an upward trend in high school students experiencing persistent feelings of sadness or hopelessness, who have considered attempting suicide, and who made a suicide plan.[3]

As medical students, physicians may recall learning about the specific details regarding rare and complex pediatric disease processes including heart disease, congenital malformations, respiratory illnesses, diabetes, and many others. However, physicians may not recall learning the top 3 leading causes of death among the adolescent and young adult age group which include unintentional injuries, suicide, and homicide.[10] With suicide as the second leading cause of death among teens, it would behoove the general pediatrician to understand how to best approach mental health concerns in this population.

According to a recent national poll of parents of adolescents ages 11-18 years, primary care providers (PCPs) ask their child about mental health concerns during 41% of their check-up visits. Fourteen percent of parents reported their child is never asked about mental health. Sixteen percent of parents reported that their teens would definitely talk to their PCPs about their mental health and 57% thought their teens would probably discuss this with their PCP.[13] This parent perspective may be helpful for providers in understanding that they are the front-lines in identifying adolescent mental health needs.

When reviewing rates of depression encountered in the primary care setting, 2 in 3 adolescents with depression are missed by PCPs and do not receive the necessary care. Of those that are identified, only half receive the right kind of care and there is often a gap in completion rates of mental health referrals.[17]

When screening adolescents for depression, pediatricians should consider the individual's risk. Many factors can play a role in the development of depression including biologic, environmental, psychologic, and genetic. Many teens are challenged with many stressors including loss, abuse, and neglect. Those struggling with chronic medical illness such as diabetes, asthma, obesity, and epilepsy are also at increased risk. Additionally, family history of depression should be considered as well as other history of co-existing mental health disorders including anxiety, ADHD, substance use, and eating disorders.[5]

An additional risk factor that pediatricians should take into consideration is one that is truly universal to all individuals—the COVID-19 pandemic. There is a growing body of literature highlighting the negative impact that the pandemic has had on the mental and physical health of many youth. Studies including parent surveys across the U.S. showed that both teen girls and teen boys were noticed to have new or worsening anxiety, depression, sleep issues, withdrawing from families, and aggressive behavior during the pandemic.[11] In another adolescent self-report study of over 700 adolescents, mental health was reported as one of their top three challenges during the COVID-19 pandemic.[14]

Over the years there has been more awareness regarding the use of social media among adolescents, and pediatricians are encouraged to ask about child and teen social media use. 93-97% of 13-17-year-old adolescents use at least one social media platform and are likely spending more than 3 hours per day on social media.[16] There are also reports of increased number of teens experiencing cyberbullying especially after the reliance on virtual school and virtual social networks since the pandemic started.[2,7]

The AAP and the USPSTF recommend that pediatricians screen adolescents for depression in youth 12 years and over during their annual care visits *and* have a plan for management when depression is identified.[6] There are many reasons why this may pose a challenge especially in a busy clinical practice setting including scope of training, experience and time. There are several resources that exist and are supported by the AAP that provide guidance for the general pediatrician. In 2018, the GLAD-PC Guidelines were updated to include evidence-based practices that are both feasible and optimal for addressing child and adolescent mental health in a primary care setting.[4,17]

Primary care providers should screen for depression in teens who present with a chief complaint concerning for a mental health concern or emotional problem, high score on a screening tool, and who are considered to be at high-risk. There are several screening tools that exist and providers should aim to use screening tools that are validated, brief, free and feasible to implement into their clinical work-flow. Specifically, for adolescent depression, brief screening tools to consider include the Patient Health Questionnaire-9 modified for adolescents (PHQ-A) or Columbia DISC Depression Scale (Table 1). Other validated screening tools do exist, however may be longer and/or require payment for use.[17]

SCREENING TOOL	USE	AGE	SELF-REPORT VS PARENT REPORT
PHQ-A (PHQ-9 modified for adolescents)	Screens for depression and suicidality	>11	Adolescent self-report
Columbia DISC Depression Scale	Screens for depression	>11	Adolescent and parent questionnaires available
Kutcher Adolescent Depression Scale (KADS)	Screens for depression	12-17	Adolescent self-report
Mood and Feelings Questionnaire	Screens for depression	8-16	Adolescent and parent questionnaires available

Table 1: Examples of Free and Easily Accessible Screening Tools for Adolescent Depression

Before a diagnosis can be made, providers should consider their differential diagnosis as there can be many overlapping symptoms among depression and other medical illnesses. Other medical causes for symptoms such as sleep difficulty, low energy, fatigue, agitation, or mood changes can be attributed to problems such as thyroid dysfunction, anemia, vitamin deficiency, malnutrition, sleep apnea, substance use/abuse. Rarely, other causes can include more chronic and severe illnesses such as autoimmune disorders, vascular disease, hematologic disease, neurologic illness, and inherited disorders. Thorough history is extremely important in order to tease out whether the patient requires a more extensive evaluation for something other than a mental health diagnosis. Equally as important is taking time to talk alone with the adolescent patient. This one-on-one time may give the provider more insight as to concerning behaviors or symptoms that the teen does not feel comfortable expressing in front of their parent or caregiver.

5 OR MORE OF THE FOLLOWING SYMPTOMS MUST BE PRESENT DURING THE SAME 2-WEEK PERIOD. AT LEAST 1 OF THE SYMPTOMS MUST BE EITHER *DEPRESSED MOOD OR LOSS OF INTEREST OR PLEASURE.* THE SYMPTOMS MUST NOT BE DUE TO OTHER CAUSES SUCH AS A MEDICAL ILLNESS OR INTOXICATION.
1. Depressed or irritable mood most of the day nearly every day
2. Decreased interest or pleasure in most activities for most of each day
3. Significant weight change
4. Change in sleep: sleeping too much or sleeping too little
5. Psychomotor agitation or retardation observed by others: difficulty sitting still or slowed movements observed by others
6. Lack of energy
7. Feelings of guilt or worthlessness
8. Difficulty with concentration
9. Thoughts of death or suicide

Table 2: Diagnostic Criteria for Major Depressive Disorder

The general pediatrician should become familiar with use of the DSM-5 when making a diagnosis of Major Depressive Disorder (MDD). Symptoms and timeframe are important in making this diagnosis (Table 2). The adolescent should have 5 or more symptoms in a 2-week period and at least one symptom should be depressed mood or loss of interest/pleasure. Other symptoms should be consistent with appetite or weight change, sleep disturbance, slowing down or restlessness, loss of energy, worthlessness or guilt, difficulty concentrating, and recurrent thoughts of death or suicidal ideation. The adolescent may not report each of these symptoms or may not meet the time frame for MDD and the provider may consider other diagnoses such as Persistent Depressive Disorder (PDD). Criteria for PDD include depressed mood or irritability for the majority of days in a 1-year period.[1]

Once the diagnosis of MDD is confirmed, it is important to categorize the severity of the depression in order optimize the treatment and management plan. History and risk factors are most important in understanding severity of illness however, screening tool scores can be helpful. For example, a PHQ-9 score of 5-9 is most consistent with mild depression; PHQ-9 score of 10-14 is most consistent with moderate depression; and PHQ-9 score of 20 is most consistent with severe depression.[17,12] It is important not to rely solely on screening tool scores because screening tools are not diagnostic. The severity of illness is also best approached by understanding the individual's level of daily functioning. For example, if the teen is able to excel in most areas such as academics, activities, family/peer relationships, then they are likely to be classified as having mild depression. For a teen who has very limited functioning or daily disruption including failing grades, loss of engagement in activities or loss of relationships they are most likely categorized as moderate to severe depression.

Treatment and management of adolescent depression should be based on the severity of the depression. For a teen with mild depression, active monitoring by the general pediatrician is a good initial step. Active monitoring includes frequent or routine check-in visits with the patient to ensure symptoms have not worsened.[4] The provider should use their clinical judgement to develop the best approach for active monitoring that is feasible for the patient, family, and for themselves as the provider. For example, using a sick-visit appointment time 2 weeks after the initial diagnosis of depression was made may be used as a brief follow-up appointment where the focus would be on addressing any mood changes or mental health concerns. Scheduling a telemedicine appointment for these types of visits can also be considered. For adolescents with more moderate or severe symptoms, one should consider and discuss the benefits of both routine therapy as well as initiating a psychotropic medication. Active monitoring by the pediatrician should still take place, however, a therapist or counselor who can provide evidence-based therapy, including cognitive behavioral therapy (CBT), should be considered as part of the management plan.[4]

Discussing therapy and psychotropic medications may feel unfamiliar and/or uncomfortable for many general pediatricians. This is why not only reviewing the mental health resources, such as the AAP mental health toolkit or the GLAD-PC guidelines in advance is important but also where practice makes perfect!...or at least makes for a more confident provider!

Evidence-based approaches for psychotherapy for adolescent depression include CBT and interpersonal psychotherapy (IPT).[4] Providers should aim to be familiar with the local resources and what types of therapy are offered either within their medical organization or within their local community. In the same way, it may be helpful to know which insurance plans therapists are in network with and who offers telemedicine appointments.

In choosing a psychotropic medication, providers should have knowledge of which psychotropic medications are FDA approved for the adolescent age group as well as the common side effect profile so they can provide appropriate anticipatory guidance to patients and families. Common side effects include headache, nausea, feeling tired, agitation, sleep and appetite changes. Typically, negative side effects occur early on after starting the medication and may go away after several days.[9] There are limited studies on child and adolescent psychotropic medication efficacy. The Treatment for Adolescents with Depression Study (TADS) is often referenced as the best gauge on medication efficacy. Currently, two SSRIs are FDA approved for this age group and include Fluoxetine for ages 8-18 years of age and Escitalopram for ages 12-17.[4] Although there are many other SSRIs and psychotropic medications often used to treat adolescent depression, starting with the FDA approved medications may align best with the comfort level of the general pediatrician.

Additionally, it is important for providers to review the boxed warning (often referred to as the black box warning) with patients and families. The boxed warning stemmed from clinical trials that were conducted in over 4000 children and adolescents where a 2% suicidality risk was identified in those taking the SSRI and in 2% who were given placebo. There were no suicides during these clinical trials.[8,15] This information allows providers to educate patients and families that the benefits of initiating medication far outweigh the risks of not treating their child's depression.

One should aim at achieving the target dose of the SSRI within 3 weeks from initiation. Monitoring medication response should occur every 1 to 2 weeks when starting and visits can be less frequent once the target dose is achieved. Once dosing is optimized, follow up visits for medication management should occur at 2 to 4-month intervals. Families and patients commonly ask how long their teen will need to be on the psychotropic medication. It is best to continue the medication for 6 to 9 months after symptom remission. When the patient is ready for discontinuation, medication should be tapered down 25% per week.[4]

If the adolescent is not showing positive response with the psychotropic medication it is okay to try the FDA SSRI that you did not try. If you are unable to achieve improvement in mood and functioning after trial of two different medications, one should consider whether they have made the correct diagnosis. This may be the best time to refer the adolescent to a psychiatrist for evaluation and medication management.

When planning for treatment and management of adolescent depression, parents may be hesitant to have their child or teen engage in routine therapy or they may be nervous about having them take a psychotropic medication. Providers should make time to listen and talk with families and patients about the risks and benefits. Combination therapy that includes both therapy and psychotropic medication yields the most benefit however, if the family agrees to start either therapy or medication, this approach can still be beneficial with positive mental health outcomes.[4]

Providers should aim towards shared decision making. Developing the treatment plan together with the teen and the caregiver to work towards unified goals can optimize mental health outcomes.

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REVIEW ARTICLE

Management of Adolescent Idiopathic Scoliosis: Latest Evidence

Yusuf Mehkri BS[1]; Eric Panther BS[1]; Caroline Davidson[1]; Jairo Hernandez BS[1]; Denna Bakhtiar[1]; Diane M. Howell MD[2]

[1]University of Florida College of Medicine, Gainesville FL, USA

[2]Department of Pediatrics, University of Florida College of Medicine, Gainesville FL, USA

ABSTRACT

Adolescent idiopathic scoliosis (AIS) is a structural spinal deformity affecting children >10-years-old without a clear pathogenesis. Appropriate early treatment of AIS is key, as untreated AIS can lead to severe cardiopulmonary dysfunction due to mechanical and structural abnormalities. Patients with mild-to-moderate AIS (10-40°) are treated with non-operative measures while patients with severe AIS (>40°) are treated surgically. Nonsurgical interventions include scoliosis-specific exercises (SSE) and bracing. These measures slowly correct the spinal deformity without the need for surgery. When the spinal deformity is >40°, spinal fusion is presently the standard of care. However, vertebral body tethering and stapling are two fusionless approaches currently undergoing investigation. Pediatric primary care providers should have an awareness of this diagnosis and its evolving treatment options to counsel families and effectively partner with orthopedic specialists in providing optimal patient care.

INTRODUCTION

Adolescent idiopathic scoliosis (AIS) is a spinal deformity with both vertebral rotation and a lateral curvature of at least 10° in children of at least ten years of age. AIS is the largest subset of spinal deformities, affecting 1-4% of adolescents between the age of 10 and skeletal maturity.[1] The need for intervention depends largely on the magnitude and progression of the curve, since the presumption is that greater curve magnitude is associated with increased risk of future negative physical and psychological consequences. These include decreased pulmonary function, increased back pain, psychosocial difficulties and decreased quality of life.[2] The level of intervention in the current management of AIS depends on both the severity of the curvature as measured by the Cobb angle and future growth potential of the patient's spine. Pediatric primary care providers must partner with orthopedic specialists to care for these patients, and an awareness of current diagnostic and therapeutic approaches is useful to primary care providers as they assess and counsel patients.

Scoliosis specific exercise (SSE) are typically recommended for patients with primary curve angles measuring 10-40° a with the goals of developing awareness of self-correcting postures and encouraging muscle strength to enhance the effects of a brace. Bracing is also recommended to these patients with the goal that the external corrective forces of the brace will halt curve progression and eliminate the need for surgical treatment in the future.[3] For patients with severe AIS, defined by curve magnitude ≥40° and skeletal immaturity, surgery is the standard of care. The gold standard for surgery is spinal fusion with pedicle screw fixation, as severe AIS can progress to cardiopulmonary dysfunction due to mechanical dysfunction of the thoracic cavity.[4,5] The two main goals of surgery are: 1) maximize curve correction and minimize curve progression to avoid the aforementioned health risks, and 2) ensure that functional mobility

and flexibility are optimized. Over the past decade alone, surgical advancements, improved radiographic techniques, and superior functional outcomes for patients have emerged. This review article will provide an overview of the latest evidence on non-surgical and surgical management of AIS.

NONSURGICAL INTERVENTIONS

Patients with curve angles of less than 10° do not meet the criteria for an AIS diagnosis. Patients with curve angles of 10-25° are considered to have mild AIS and will generally be monitored with serial x-rays at 3-, 6-, or 12-month intervals. Those with moderate AIS have curve angles of 25-40° and will also undergo serial x-rays to track the progression of their scoliosis. Besides watchful waiting, nonsurgical interventions for patients with mild to moderate AIS (10-40°) include scoliosis-specific exercises (SSE) and bracing (Table 1).

TREATMENTS	ADVANTAGES	DISADVANTAGES
Scoliosis Specific Exercises	Evidence for decreased Cobb angles, lower pain scores, improved self-image, and a decrease in waist asymmetry	Insufficient evidence to suggest that improvement is more significant than no treatment at all
Bracing Therapy	High success rate for preventing curve progression in years following treatment	Usually only for patients with moderate AIS; brace must be worn the majority of the day which leads to low compliance rate

Table 1: Non-Surgical Interventions for Moderate AIS

In mild to moderate AIS, specific exercises are both as an adjunct and alternative to bracing. There are many SSE regimens around the world, with some notable ones including the Scientific Approach to Scoliosis from Italy and the Schroth approach from Germany, which are scoliosis-specific intensive inpatient rehabilitation programs with certified therapists.[6] The exercise prescription and regimen depend on the severity of curve. However, all regimens include both static and dynamic movements. Exercises recommended for all curve types include a "side-lying shoulder contraction" where the patient lies on their side with their waist elevated by a high-density foam roller. Other exercises require the patient to practice balancing on a stability ball or practice "conscious walking", walking while auto-correcting spinal asymmetry.[7] These SSE regimens have been assessed in randomized controlled trials with impressive results, including decrease in Cobb angles, lower pain scores, improved self-image, and a decrease in waist asymmetry.[8] However, reviews have shown that there is insufficient evidence to suggest that the Schroth and the Scientific Approach to Scoliosis improve outcomes in AIS compared to no intervention.[9] There is a need for more and varied studies investigating the effectiveness of SSEs in improving spinal curvature in AIS patients.

Bracing therapy is primarily indicated for patients with moderate AIS (curve angle: 25-40°) to prevent the scoliosis from progressing over time. Most bracing recommendations suggest the brace should be worn at least 16 hours per day, with the treatment protocol lasting from 2 to 4 years or until skeletal maturity. Although these braces are widely prescribed, these devices have low compliance rates.[10] At present, the literature remains inconclusive with respect to the efficacy of bracing for skeletally immature adolescents with mild AIS. Danielson et al.[11] conducted a 16-year follow-up study of 92 moderate AIS patients and found no curve progression in patients primarily treated with a brace, but an average curve progression of 6° for the 70% of patients in the observational group who were not treated surgically or with a brace. On the other hand, a meta-analysis by Dolan and Weinstein[12] found no significant difference between surgical rates after bracing compared to observation. Given the intense time requirement and discomfort of brace treatment, it is not surprising that noncompliance is one of the most prevalent risk factors in the progression of scoliosis. Although the results for bracing therapy effectiveness are mixed, a recent meta-analysis showed that adding SSE to bracing therapy improved patient outcomes compared to bracing alone.[13] Rigorous, prospective studies of the individual and combined effectiveness of bracing and SSEs on curve progression and occurrence of surgical intervention are needed.

SURGICAL INTERVENTION

Spinal fusion

Currently, the most common surgical approach for the treatment of AIS is posterior spinal fusion (PSF). PSF allows for a strong, stable correction of severe AIS, while providing significant improvements in all domains of the Health-Related Quality of Life (SRS-30) questionnaire among adolescents with all types of AIS.[14] A caveat is that this procedure is not the best option for a subset of patients who are skeletally immature and experience progressive angular and rotational spinal deformity (also known as the crankshaft phenomenon) after undergoing PSF. This phenomenon occurs because the anterior elements of the spine continue to grow in patients with high growth potential who undergo posterior-only fusion.[15] Potential adverse outcomes include impairment of pulmonary

function and revision surgery, which can be avoided with a combined anterior and posterior fusion approach (APSF).[15] Sponseller et al.[16] conducted a two-year follow-up on 29 skeletally immature patients who had undergone either PSF or APSF. They showed that although the APSF group had significantly longer hospital stay and operative time, this group had no patients go on to >10° curve progression as compared to 35% of patients in the PSF group. For the general AIS patient population, when it comes to deciding between performing either PSF or APSF, a recent meta-analysis looked at 872 patients across ten studies from 1976 to 2013 and found the two to be equally effective when it came to curve correction. However, the posterior-only approach also showed significantly less blood loss, fewer complications, shorter operative and recovery time, and a level of effectiveness that deemed an additional anterior surgical intervention unnecessary.[17]

Minimally invasive spinal surgery (MIS), which employs smaller incisions in order to minimize injury to the paraspinous muscles and other structures, has also shown promising results and may become an alternative to the gold standard in the coming years. This approach has long been effective for adult spine pathologies and deformities and has just started to make its way to the AIS population.[18] Sarwahi et al.[19] showed that patients who underwent MIS achieved comparable curve correction and accurate screw placement as patients who underwent PSF. However, there was no difference in level of pain or hospital stay as was expected. Zhu et al.[20] carried out a similar study soon after with AIS patients and obtained better results including decreased radiation exposure, blood loss, and post-operative pain. Although both studies did show a significantly longer operation time for MIS, this can be partially attributed to the inherent learning curve. As more surgeons are trained in MIS, and more long-term data is collected, this technique may become more effective at treating the technically challenging spinal deformities of AIS patients.

Anterior Vertebral Body Tethering

Anterior vertebral body tethering (VBT) is a fusionless approach to treating AIS patients by slowing down vertebral growth on the convex side in the hopes of equilibrating the height on both sides of the vertebral body.[21] Newton et al.[22] showed that asymmetric spinal tethering can result in growth modulation and spinal deformity in an immature bovine model, and another study[23] showed that pre-tensioning of the tether can modulate growth while maintaining disc health, spinal motion, and stiffness. Because this technique relies on growth modulation, it is ideal for skeletally immature AIS patients with flexible curves.

Samdani et al.[24] was the first group to retrospectively evaluate outcomes with a large cohort (n=32) of AIS patients and found very promising results. At one-year follow-up, there was a 58% decrease in thoracic curve magnitude and an average 6° reduction in thoracic axial rotation. A two-year follow-up was conducted on eleven of these patients showing further progressive improvements in both measures.[25] Overcorrection was a concern in a few patients who had to undergo revision surgery to loosen the tether, however, this was expected given the early experimental nature of this procedure. Takahashi et al.[26] performed a study with 23 adolescent idiopathic scoliosis patients which determined the rate of kyphosis correction to be approximately 1.8° per segment per year for the first 2-3 years following anterior VBT.

Newton et al.[27] conducted a two to four-year follow-up and obtained interesting results. Although 59% of the 17 patients studied were considered clinically successful because they had achieved curves measuring <35° and did not require PSF, many patients either underwent revision surgery for tether-related issues or experienced curve progression around 18 months post-operation. The authors used these findings to suggest that more data ≥ 2 years post-operation and up to skeletal maturity are necessary to better understand how patients respond to VBT. It is important to keep in mind that three patients included in this study had syndromic scoliosis (not idiopathic), and that most of these patients would not have been considered ideal candidates for VBT considering their curves demonstrated <50% flexibility.[21] Newton et al.[27] more recently demonstrated in a 14-patient study of all idiopathic scoliosis patients that anterior VBT can cause the periapical vertebrae and discs to grow asymmetrically leading to the desired reduction in disc height on the convex side.

Vertebral Body Stapling

Vertebral Body Stapling (VBS) is another proposed fusionless technique for correction of AIS.[28] This procedure is performed by placing staples on the anterior vertebral growth plates causing restrained growth on the convex side and natural growth on the concave side of the spine.[4] Sunni et al.[28] evaluated the efficacy of VBS in bovine calves and showed that VBS appears to reduce spinal stiffness but can cause physeal damage. However, Murray et al.[29] evaluated 7 patients with AIS who underwent VBS for correction of their spinal curvature. The average rate of growth on the stapled verses unstapled side were 0.86 mm/year and 0.83 mm/year respectively. This similar rate of growth demonstrates that in its current form VBS cannot be used for severe scoliosis. Trupia et al.[30] concluded in a 10 AIS patient study that VBS does not appear to be more beneficial than bracing. VBS also did not affect the percentage of patients who eventually required surgical intervention for their worsening scoliosis. Additionally, they showed that VBS and bracing resulted in similar levels of spinal deformity correction. In conclusion, VBS does not currently appear to be not a viable option for surgically correcting AIS because it delays adequate treatment (Table 2).

TREATMENTS	ADVANTAGES	DISADVANTAGES
Spinal Fusion	The most common surgical technique; patients show significant improvements in Quality of Life scores	Not idea for skeletally immature patients; multiple operations are sometimes required
Anterior Vertebral Body Tethering	Most patients are considered clinically successful and did not require a fusion surgery	This technique relies on growth modulation and is only ideal for skeletally immature AIS patients
Vertebral Body Stapling	This technique is fusionless and shows evidence for reducing spinal stiffness	Shows similar levels of spinal deformity correction to bracing; may cause physeal damage

Table 2: Surgical Interventions for Severe AIS

CONCLUSION

Adolescent idiopathic scoliosis impacts many children between the age of 10 to skeletal maturity and is associated with pulmonary dysfunction, back pain, and negative psychosocial consequences. Treatment over the last decade has largely been posterior spinal fusion which requires instrumentation and considerable risk of revision surgery, increasing the risk of infection and complications. However, novel nonsurgical and surgical treatments have recently emerged as promising therapeutics for AIS. Scoliosis specific exercises appear to help with deformity and pain in patients with moderate scoliosis, whereas bracing therapy has demonstrated mixed results. The combination of the two has been shown to be effective. Surgical treatment appears to be moving away from traditional posterior spinal fusion and toward minimally invasive approaches to the procedure as well as novel vertebral body tethering due to its high success rate and lower risk of complications. The treatment method physicians propose to their patients should be tailored to the patient's unique clinical picture and goals. Pediatric primary care providers should be aware of current research outcomes and treatment trends to assist in referring patients for the most evidence-based care.

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RESIDENT ARTICLE

Hyperinsulinemic Hypoglycemia in an Infant with Partial Trisomy 13

Aashima Pandhi, MD[1]; Martina Drawdy, MD[2]; Callah Antonetti, MD[3]

[1]Department of Pediatric Hematology and Oncology, Case Western Reserve University School of Medicine, Rainbow Babies and Children's Hospital, Cleveland, OH

[2]Department of Pediatric Endocrinology, University of Florida, Ascension Sacred Heart, Pensacola, FL

[3]Department of Pediatrics, University of Florida, Ascension Sacred Heart, Pensacola, FL

ABSTRACT

Hyperinsulinemic hypoglycemia is the most common cause of hypoglycemia that persists in infants, though clinical signs of hypoglycemia in this age can be subtle. Persistent hypoglycemia in infants can lead to neurologic consequences if not promptly identified and treated. Hyperinsulinemic hypoglycemia has also been associated with multiple genetic syndromes. A high index of suspicion is required to make the diagnosis of hyperinsulinemic hypoglycemia, as management differs from other causes of hypoglycemia. In this case report, we describe an 8-week-old infant with known partial trisomy 13 with persistent hypoglycemia despite intravenous dextrose boluses, found to have hyperinsulinemic hypoglycemia.

BACKGROUND

Hyperinsulinemic hypoglycemia (HH) is a condition characterized by increased insulin secretion from pancreatic beta-cells, even when blood glucose levels are low (serum glucose < 50 mg/dl). In infants and children, it is considered to be the most common cause of persistent hypoglycemia.[1] If blood glucose levels remain low and there are no other cellular substrates available such as lactate or ketones, there is an increased risk of neurological damage in these patients in the setting of cellular energy failure. HH has been associated with several genetic syndromes like Beckwith-Wiedemann Syndrome, Sotos Syndrome, Simpson-Golabi-Behmel-Syndrome, Kabuki Syndrome, Costello Syndrome, Mosaic Turner Syndrome, and has rarely also been reported in cases of Trisomy 13.[1] Here we present a case of an 8-week-old male born at 37 weeks gestation with partial trisomy 13 due to an unbalanced translocation of chromosome 13 and 17, found to have HH.

Objective: To describe the presentation, pathophysiology, and management of an 8-week-old infant with partial trisomy 13 presenting with apnea and feeding difficulties, found to have hyperinsulinemic hypoglycemia.

SUBJECT PRESENTATION

An 8-week-old male born at 37 weeks gestation following a pregnancy complicated only by multiple urinary tract infections, presented to the emergency department with feeding difficulties and apneic episodes. He had a history of partial trisomy 13 due to an unbalanced translocation between chromosomes 13 and 17, a patent foramen ovale and a small ventricular septal defect, and a brief neonatal ICU admission after birth for hypoglycemia requiring orogastric feeds and intravenous dextrose infusion. The hypoglycemia resolved without any additional evaluation. After discharge, he developed feeding difficulties and often had associated coughing, gurgling, and choking spells. An outpatient swallow study showed silent aspiration. He also developed self-resolving episodes of apnea associated with perioral cyanosis. On initial presentation to the emergency department for these symptoms, his examination was normal except for subtle dysmorphic features, including low set ears, a broad nasal bridge, micrognathia and hypospadias. There were no obvious midline abnormalities, no hepatomegaly and the penile size was normal for age. Complete blood count and comprehensive metabolic panel were normal on admission except a serum glucose of 48 mg/dL. He received intravenous fluids containing 5% dextrose and blood glucose normalized. He had an upper GI series done which showed intestinal malrotation and tracheomalacia. He was started on nasogastric bolus feeds. Several hours after admission he had an episode of left eye deviation, upper extremity stiffening and perioral cyanosis concerning for seizure. Serum glucose was 43 mg/dL at the time of this episode, at which point critical hypoglycemia labs were obtained. He was noted to have an elevated insulin level of 30.7 IU/ml, beta-hydroxybutyrate level 0.27 mmol/L, cortisol level 12.77 mcg/dL and growth hormone level 1.84 ng/ml. Additional evaluation for seizure including prolonged EEG was normal and a MRI brain did not reveal structural brain abnormalities, patient had cavum septum pellucidum and a normal corpus callosum.

Over the next 12 hours, the patient received three 10% dextrose fluid boluses which transiently improved blood glucose levels before hypoglycemia recurred. Pediatric Endocrinology was consulted, and he was diagnosed with HH. He was started on continuous nasogastric feeds and oral diazoxide 10 mg/kg/day divided TID to which he responded well with resolution of hypoglycemia. It was also recommended to avoid additional bolus dextrose infusions to prevent worsening of hypoglycemia, due to increased insulin secretion in response to the sudden exposure to increased glucose concentrations. Additionally, during his hospitalization, he underwent a Ladd's procedure and gastrostomy tube placement for the malrotation and aspiration. A bronchoscopy was done which showed severe tracheomalacia and left bronchomalacia, and he required high-flow-nasal cannula support for persistent apnea episodes. He developed significant generalized edema, a known side effect of diazoxide, treated initially with furosemide. Subsequently, thiazide diuretics were added to his regimen. While his blood glucose levels stabilized with gastrostomy tube feedings and diazoxide, he was ultimately transferred to a specialized children's center for definitive management of recurrent apnea given underlying airway abnormalities.

DISCUSSION

Glucose is one of the body's major energy substrates, and blood glucose concentration is regulated by metabolic hormones. Insulin is the hormone responsible for decreasing blood glucose levels. Blood glucose levels are increased by catabolic hormones including glucagon, cortisol, and catecholamines.[1]

Hyperinsulinemic hypoglycemia is the most common cause of persistent hypoglycemia in infants.[1] In HH, there is an increase in insulin secretion from pancreatic beta-cells, even when plasma glucose concentrations are low. This condition can be potentially life-threatening, leading to significant neurological damage due to the lack of glucose as fuel for neurons.[2]

HH can be transient or permanent in the pediatric population. Transient forms usually resolve within a few days to a week, although in some children it can persist for up to six months.[1] The transient forms of HH have been associated with intrauterine growth restriction, perinatal stress, erythroblastosis fetalis, and maternal diabetes mellitus.[1,3] The permanent form of HH occurs when children continue to require treatment beyond six months of age. The permanent cause is most commonly congenital, to date there have been at least 15 genes associated with congenital hyperinsulinemic hypoglycemia including ABCC8, KCNJ11, GLUD1, GCK, HADH, SLC16A1, UCP2, HNF1A, HNF4A, HK1, PGM1, PMM2, FOXA2, CACNA1D, and EIF2S3.[3] There are three histological forms of congenital hyperinsulinemic hypoglycemia (CHH). Focal CHH occurs when one area of the pancreas has abnormal pancreatic beta-cells, diffuse CHH occurs when all pancreatic islets are affected, and atypical CHH occurs when there is a mosaic pattern of focal and diffuse CHH.[1,3]

HH most commonly presents in infancy and childhood. In infancy, HH can present as irritability, jitteriness, or poor feeding.[3] Our patient presented with poor feeding and post-prandial apneic episodes. However, as apnea persisted after stabilization of blood glucose levels, his presenting symptoms were likely multifactorial and also related to aspiration and airway malacias.

HH can become apparent during periods of fasting but may also be precipitated by a meal.[3] Hypoglycemia that occurs while an infant receives an intravenous dextrose infusion is strongly suggestive of hyperinsulinemic hypoglycemia. HH can be diagnosed by the presence of detectable insulin or C-peptide in the setting of hypoglycemia with simultaneous low or undetectable levels of other cellular fuels like ketones.[4]

The management of HH involves achieving normoglycemia acutely with the help of continuous enteral feeds and/or continuous intravenous fluids containing dextrose and if severe, the use of intramuscular or subcutaneous glucagon, and maintaining normoglycemia chronically with the help of medical or surgical interventions. Diazoxide is the first drug of choice. Its mechanism of action is promotion of the opening of potassium-gated ATP channels, thus inhibiting the pancreatic secretion of insulin.[5] Nifedipine and octreotide have been reported to work in diazoxide-unresponsive HH.[3] Long acting somatostatin analogues like lanreotide and mTOR inhibitors like sirolimus have also recently shown to be beneficial in diffuse-CHH.[6] In cases unresponsive to medical management, surgical removal of part of the pancreas in focal-CHH, or near-total pancreatectomy in diffuse-CHH are the treatment modalities of choice.[3]

CONCLUSION

Hyperinsulinemic hypoglycemia is caused by increased insulin secretion by the pancreas in the context of low plasma glucose concentrations. It has been reported in several genetic syndromes to date and there have been reports of the same being managed by continuous glucose infusions and medical management as was done in our patient. The most critical factor in management of HH is the avoidance of wide fluctuations in the serum glucose by avoiding boluses of dextrose or a rapid wean of the supplemental source of glucose, as this can worsen hypoglycemia in response to the surge of insulin secretion. Patients with HH require high diagnostic suspicion and early intervention due to the risk of permanent neurological damage with recurrent hypoglycemia early in life.[2] These patients benefit from home blood glucose monitoring and careful medication dose titrations based on clinical response, and upon discharge from the hospital should be followed closely by a pediatrician and a team specialized in pediatric endocrinology.

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STUDENT ARTICLE

Red Eye: An Unusual Suspect

Anusha S. Tuli[1]; Alexander H. Dang[2]; Ruchita Kachru, MD[3]; Ankit Shah, MD[4]
[1]Barnard College, Columbia University, New York, New York
[2]Harvard University, Cambridge, Massachusetts
[3]Department of Pediatrics, University of Florida, Gainesville, Florida
[4]Department of Ophthalmology, University of Florida, Gainesville, Florida

INTRODUCTION

Red eye is common in children and is often associated with viral or allergic conjunctivitis. In these cases, the condition is usually bilateral and associated with tearing. The list of other conditions leading to red eye is long and includes infectious, inflammatory, autoimmune, and traumatic causes. Herpes simplex keratitis (HSK) is one of the more common infectious causes of red eye in children but usually presents as unilateral blepharoconjunctivitis with eyelid vesicles and a follicular conjunctivitis. Corneal involvement in childhood is rare as it is usually associated with recurrent disease that occurs in adulthood. The classic dogma is that herpes simplex virus (HSV) type 1 causes infections above the waistline while HSV type 2 (HSV-2) causes genital herpes as well as congenital herpes as the neonate gets infected passing through the infected birth canal. Here we present a case report of a young girl with a corneal ulcer caused by HSV-2.

CASE REPORT

An 11-year-old female was referred to the emergency department (ED) by an optometrist as they were concerned about a corneal ulcer in her right eye. Approximately three weeks prior to presentation, the patient had developed a foreign body sensation in her right eye associated with some redness. Her mother assumed she had pink eye and had started over the counter lubricating drops as well as "pink eye" drops without improvement. Subsequently, the patient noted blurry vision in that eye that appeared to be worsening, so she went to an optometrist who prescribed moxifloxacin and prednisolone acetate eye drops. She was then sent to a second optometrist who was concerned about a corneal ulcer and sent her to the ED.

On presentation to the ED, the patient complained that she had persistent foreign body sensation in the right eye associated with redness, irritation, and decreased vision. She denied contact lens wear but did wear glasses for vision correction for astigmatism and refractive error. There was no history of trauma or other eye problems in the past. Her past medical history was only positive for attention deficit hyperactivity disorder and asthma and negative for fever blisters. She had no allergies and review of systems was completely negative. She was in school, denied being sexually active, and lived with her mother, older sister, and the sister's boyfriend.

On examination, she appeared healthy and well-nourished and the only pertinent abnormal findings were in the right eye. The vision in the right eye was hand motions only, while the left eye was 20/25. Intraocular pressure was slightly decreased in the right eye at 16 mm Hg compared to 23 in the left eye. Pupils, extraocular movements, and external ocular examination were normal with no rash on the eyelids. On slit lamp examination of the right eye, she was noted to have a protective ptosis, follicular conjunctivitis and diffuse haze of the cornea (Figure 1). There were granulomatous keratic precipitates in a ring fashion on endothelium (Figure 2), limbal elevation superiorly (Figure 3), and a small dendritiform lesion centrally. The anterior chamber could not be viewed due to the corneal haze but the lens appeared clear. There was no view of the fundus due to media haziness. The left eye was completely within normal limits.

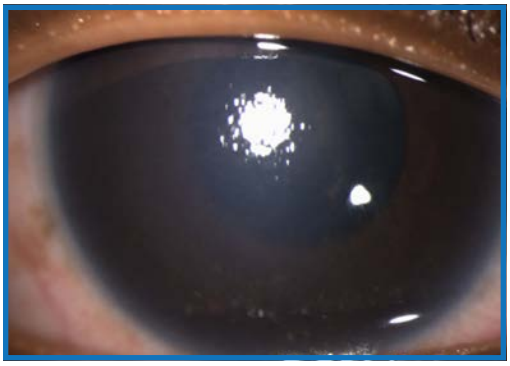

Figure 1: Right cornea showing diffuse haze with limited view of intraocular structures

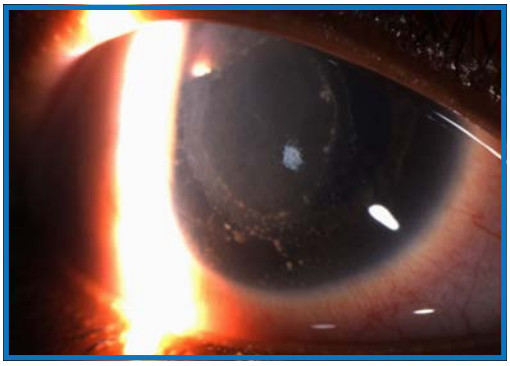

Figure 2: Indirect illumination showing a ring of keratic precipitates on the endothelium

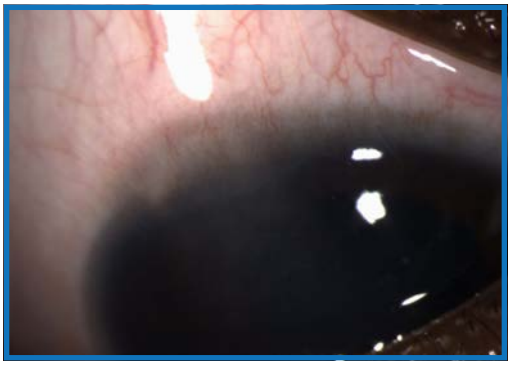

Figure 3: Inflammation of the corneal limbus

Given the findings, the initial differential diagnoses considered were anterior uveitis from sarcoid, tuberculosis, syphilis, or Lyme disease or herpes simplex or zoster keratitis. Conjunctival swabs for PCR for herpes simplex virus (HSV) and varicella VZV and a chest X-ray were obtained and blood was drawn for laboratory testing including CBC with differential, HLA-B27, rheumatoid factor, C-reactive protein, erythrocyte sedimentation rate, syphilis tests, Lyme antibodies, Lysozyme, ACE, ANCA, ANA, and QuantiFERON-TB Gold. The patient was started on valacyclovir 1 gm TID orally and cyclopentolate 1% TID topically OD due to the high suspicion for a herpetic keraitis. The steroid and antibiotic eye drops were continued.

The patient was seen in the eye clinic the next day with an unchanged exam other than resolution of the corneal dendrite. The PCR test for HSV-2 was noted to be the only positive test at this time. The corneal sensation was tested in the right eye during this visit and was found to be diminished compared to the left eye. A B-scan ultrasound was performed to evaluate the posterior chamber and was found to be normal with no evidence of inflammation. An anterior segment ocular coherent tomography was performed and confirmed the keratic precipitates on the endothelium (Figure 4, arrow). Patient was continued on valacylovir and the prednisolone acetate was increased to every 2 hours while awake. Cyclopentolate was continued and moxifloxacin was discontinued.

A long discussion with patient and mother was undertaken as HSV-2 infection is usually sexually transmitted. Patient denied being sexually active or being abused. However, given the age of the patient, the department of child protection services was consulted who did not find any evidence of abuse. It was therefore assumed that she had likely contracted HSV-2 during birth and this had stayed latent in her trigeminal ganglion and recurred at this time.

Patient returned one week later and indicated that she was doing much better. Vision had improved to 20/100 with decrease in the keratic precipitates and corneal edema. The medications were continued. Six weeks following the initial visit, the vision had improved to 20/25 with faint pigmented keratic precipitates on the endothelium and mild corneal haze (Figure 5). The valacyclovir was decreased to 500 mg daily and the prednisolone was tapered gradually to one drop on alternate days over the next 4 months. However, at that dose, the patient's vision declined to 20/100 and it was noted that she had increased inflammation and corneal edema. The prednisolone was increased to twice a day for a month and then decreased back to once a day after another month (when the eye was noted to be quiet again) with plans to continue that treatment long-term along with valcyclovir 500 mg daily long-term to prevent recurrences.

DISCUSSION

Herpes simplex is a double stranded DNA virus that belongs to the Herpesviridae family, which includes other members such as herpes zoster virus and cytomegalovirus.[1] Common to all the members of the family is the condition of latency where the virus, upon entering the body, resides in either the nervous or hemolymphatic system permanently in a quiescent state.[2] A change in the immunological status of the host results in reactivation of the virus (lytic phase), causing recurrent disease.[3] In some cases, such as in herpes zoster virus, reactivation usually results in immunity for a period, during which the virus becomes latent again. However, in the case of herpes simplex virus, reactivation occurs frequently, and although the virus becomes latent between reactivations, the recurrence rate increases with increased number of recurrences.[4]

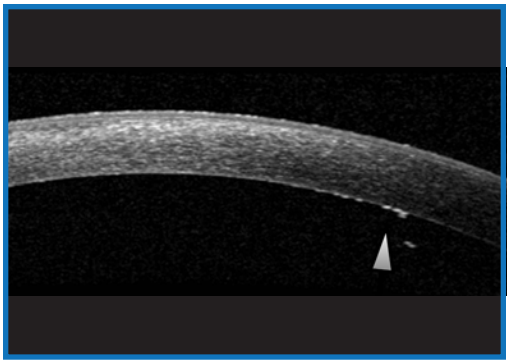

Figure 4: Ocular coherent tomography of the cornea confirming the location of the inflammatory deposits on the endothelium

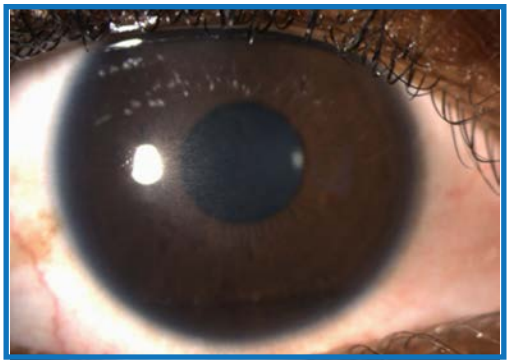

Figure 5: Resolution of the corneal haze and keratic precipitates after treatment with steroids and antivirals

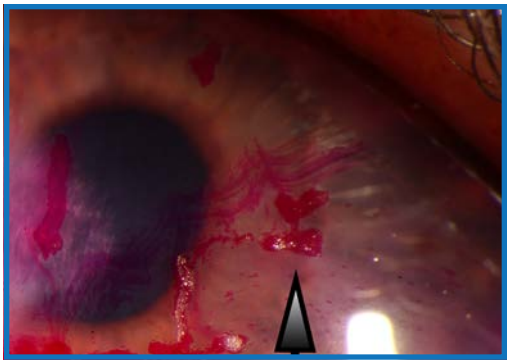

Figure 6: Classic epithelial HSV with dichotomous branching and terminal bulbs

Herpes simplex has two members: HSV type -1, which usually resides latent in the trigeminal ganglion most commonly causes oral, nasal, and ocular disease and HSV-2, which usually lies dormant in the sacral ganglia, commonly causes genital herpes and is often spread through sexual activity.[4] HSV-2 affects the eyes less frequently than HSV-1 and is thought to cause more severe disease. It is unknown whether ocular disease with HSV-2 is caused by direct contact of the ocular mucus membranes with infected secretions from the sexual partner, or whether it is due to self-inoculation from genital herpes. HSV-2 may also be transmitted to babies as they pass through the birth canal of infected mothers, and this is the most likely method of infection in this child. Research has shown that latently infected individuals asymptomatically shed the virus in their secretions frequently, and that this is the primary mode of transmission.[5]

Unilateral blepharoconjunctivitis characterized by a vesicular dermatitis of the eyelids with an associated follicular conjunctivitis is the most common ocular manifestation of HSV in children.[6] This presentation is commonly misdiagnosed as impetigo, "pink eye," staphylococcus blepharitis, or phylectenular Keratoconjunctivitis especially if the cutaneous lesions are sparse and overlooked. These lesions usually resolve spontaneously without sequelae. Subsequent recurrent disease can manifest as blepharoconjunctivitis, but more frequently seen as infection of the cornea known as keratitis. Unlike adults, both recurrent disease and bilateral disease is much more common in children especially if the child has a history of atopic disease and asthma.[7]

HSV keratitis can be subdivided into epithelial, stromal, and endothelial, though multiple layers of the cornea may be affected at the same time.

1. Epithelial keratitis: The prototypical lesion is a dendrite (branching lesion), on the corneal surface. Dendrites classically have dichotomous branches and terminal bulbs at the end of each branch (Figure 6). The virally infected cells are at the border of the dendrite with an epithelial defect centrally.[8] Occasionally, in immunocompromised individuals, or those on topical steroids, the lesion enlarges and becomes a geographic ulcer.[8] These lesions usually take longer to resolve with treatment and can have underlying inflammation. Epithelial disease is treated with either oral or topical antiviral medication with adjunct surgical debridement. (Table 1).[9]

ORAL MEDICATION	TREATMENT DOSE	PROPHYLACTIC DOSE
Acyclovir	400 mg 5 times a day	400 mg BID
Valacyclovir	500 mg TID	500 mg daily
Famciclovir	250 mg TID	250 mg daily
TOPICAL MEDICATION	**CONCENTRATION**	**DOSE**
Trifluridine eye drops	1%	Every 2 hours while awake
Ganciclovir gel	0.15%	5 times a day

Table 1: Oral and topical antiviral medications commonly used for HSV keratitis

2. Stromal keratitis: This is usually differentiated into two types: with and without necrosis. Stromal disease without necrosis is thought to be a host immunological response to viral antigen in the cornea rather than to live virus. It is manifested by patchy inflammation in the corneal stroma (interstitial keratitis) without involvement of the epithelium or endothelium.[10] When treated early, it resolves completely without residual scarring. However, untreated interstitial keratitis can lead to permanent corneal vascularization that can affect the vision and lead to lipid keratopathy due to serum leaking out of these vessels.[11] Lipid keratopathy is one of the major causes of vision loss from HSV keratitis. Unfortunately, the corneal scarring and opacification usually associated with untreated stromal keratitis in young (less than 8-years-old) pediatric patients can have devastating impact on vision as it predisposes these patients to deprivational and astigmatic amblyopia.[12] Stromal disease with necrosis (necrotizing keratitis) is thought to occur in patients that have had several bouts of recurrent disease in which there is an immune response to viral antigen deposited from previous bouts of HSV in addition to live virus.[13] This can lead to severe inflammation in the cornea and ulceration that can cause the cornea to perforate. This needs to be treated urgently with oral antivirals as well as steroids but often has poor outcomes due to residual scarring and corneal thinning.[14]
3. Endotheliitis (disciform keratitis): This is an inflammatory response to viral antigen or live virus in the endothelial layer of the cornea, and can be described as disciform, diffuse or linear based on its appearance.[15] The endothelium cells function by dehydrating the cornea to maintain its clarity. Any insult to the endothelial cell function (through inflammation or infection) results in swelling and thickening of the cornea. The inflammation associated with HSV endotheliitis presents as granulomatous keratic precipitates, translucent spots of inflammation usually in a ring shape on the inner layer of the cornea.[16] Early treatment with topical steroids is crucial in treating this condition, reducing corneal edema, and preventing permanent vision loss.[17]

CONCLUSION

This patient had a combination of follicular conjunctivitis and endotheliitis, which is an unusual presentation. Therefore, she was treated with therapeutic doses of valacyclovir as well as high doses of steroids to treat the infectious and inflammatory components, with an excellent outcome. Given the severity of the initial episode, the plan was to keep her on a prophylactic dose of valacyclovir long-term. Although we attempted to taper off her steroids gradually, she had recurrence of her inflammation upon decreasing it to alternate days. This is likely because there is persistent viral antigen in the endothelium and she will require a low dose of topical steroids long-term to prevent her inflammation from flaring up. Unfortunately, even prophylactic antivirals do not eliminate the risk of recurrence, and she is at high risk to have additional episodes.[18] She and her mother were therefore counseled that she would need frequent eye exams and that they should return immediately if she developed a red eye in the future.

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