PALLIATIVE CARE
CASE OF THE MONTH

"The Crying Child"
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Case: Baby N is a 5 month old boy with Cri-du-Chat syndrome. Cri-du-Chat is a deletion of the 5p chromosome, characterized by a cat like cry, hyperactivity, feeding problems, and severe cognitive, motor, and speech delays but is not a life-limiting illness. He has multiple complications including a heart defect, laryngomalacia, and respiratory failure secondary to upper airway obstruction. The palliative care service was consulted to help with his neuro-irritability. Neuro-irritability is when a child appears irritated (crying, writhing etc.) and/or has persistent muscle spasms and dysautonomia, even after all identifiable sources of pain have been treated. Baby N's neuro-irritability was apparent when he was irritable for 1-2 hours and unable to be soothed with normal techniques including but not limited to holding, swaddling, feeding, and cleaning his diaper.

Discussion: Treatment of Neuro-irritability:
Neuro-irritability occurs in neurologically impaired children who are unable to voice their symptoms. Most patients are infants, symptoms start at 3 months and typically worsen during the first year. The theory is that it is due to aberrant brain development with autonomic instability stemming from the hypothalamus. These patients have no identifiable nociceptive source of pain. The patient's symptoms may indicate a central pain or visceral hyperalgesia such as pain with feedings, flatus, and bowel movements. Other symptoms include muscle spasms or dysautonomia. Unfortunately, on review of the literature there is no documented prevalence or incidence.
The current theory of neuro-irritability is that the nerves are firing spontaneously like we see in adults with peripheral neuropathy.
There is little literature discussing the topic. Most of the data is based on case reports. Gabapentin, a medication that was developed as an anti-seizure medication, is the first line therapy [1] (based on case reports). It is postulated that the gabapentin works on the calcium channels to reduce the nerve irritability. Side effects of gabapentin include somnolence, and to avoid sedation the medication is titrated starting at 5mg/kg daily with daily increases to TID dosing. Maximum dosing is 45-60 mg/kg/day with slow titration to that dose.
Clonidine, an alpha-2 agonist that works centrally and inhibits sympathetic outflow, has also been used as an agent in neuro-irritability [2]. Studies have shown that it reduces hypersensitivity by immunomodulatory effects [3]. Clonidine has been used with some success in children and should be considered if gabapentin is not effective or tolerated.
The starting dose for clonidine in children is 0.002mg/kg nightly. The side-effect profile is similar to gabapentin and includes sedation and constipation.
Tricyclic antidepressants (TCAs) have also been described anecdotally for controlling neuro-irritability [4]. The recommended starting dose for TCAs is 0.2mg/kg nightly. TCAs are known to prolong the QTc interval and requires monitoring with repeat EKGs. Overall TCAs are being used less since gabapentin and clonidine are effective in most cases.
In terms of non-pharmacologic treatment options, parents are to be encouraged to monitor their children for symptoms of pain or discomfort and what relieves them [5]. There are no clear studies of CAM therapies

Resolution of the Case: During the course of being seen by the palliative care service, he was started on Gabapentin and Clonidine. In addition, he also was held daily for about an hour. The patient became more calm and adept to being held. He was controlled on that regimen until he went for hernia repair. During the post -operative period the patient was controlled on minimal amounts of morphine for the visceral pain. His irritability continued to be controlled on the above mentioned regimen.

References:

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2. Hauer, J., et al., Pediatric Pain and Symptom Management Guidelines. 2011.
3. Romero-Sandoval, A. and J.C. Eisenach, Perineural Clonidine Reduces Mechanical Hypersensitivity and Cytokine Production in Established Nerve Injury. Anesthesiology, 2006. 104(2): p. 351-355.
4. Wood, A.J., C.B. Berde, and N.F. Sethna, Analgesics for the treatment of pain in children. New England Journal of Medicine, 2002. 347(14): p. 1094-1103.
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Personal details in the case published have been altered to protect patient privacy.