LETTERS

To the editor: Regarding the article on anesthesia in Freeman-Sheldon syndrome (AANA Journal, February 2020, Vol. 88, No. 1): It is encouraging to see this exquisitely rare condition correctly identified in the literature. Unfortunately, this article is somewhat unclear, apparently resulting from the authors’ omission of recent literature, especially clinical recommendations for anesthesia management authored and open peer-reviewed by providers who each have multiple decades of experience caring for these challenging patients.

Though they indicate no apparent association exists, the authors suggest a predisposition to malignant hyperthermia (MH) in the syndrome, but it has also been observed to be resolved by administration of ibuprofen. These hyperpyrexia events, which may include tachycardia and increased muscle rigidity, have also been seen in settings where an MH protocol was followed and in non-operative stress situations, such as physical or mental stress well beyond what the individual typically experienced. It seems, then, these hyperpyrexia events may not represent true MH events.

The authors also cite the unsubstantiated frequency of 1:1 million. They also state FBS may be slowly progressive—for which there is no evidence—and inherited in an autosomal recessive pattern, which is no longer accepted. In discussing major clinical features of FBS, they omit the clinical diagnostic criteria, while referring to a short-webbed neck and kyphoscoliosis, which are features required and more frequently seen in Sheldon-Hall syndrome (SHS). SHS is a similar appearing but pathologically distinct condition with a more moderate course. Management of both patients described included fentanyl for induction, which is concerning. As the authors correctly state, post-operative pulmonary complications are a major concern in these patients. Respiratory depression, exacerbated with opiates, is a risk factor increasing this possibility. If opiates are used, long-acting forms—such as fentanyl—should be avoided. The authors also suggest that cardiac involvement is possible in this syndrome, for which there is no supporting evidence. This article illustrates the perils of describing a rare condition.

REFERENCES

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Response: We would like to thank Poling and Dufresne for interest in our work and their inputs for our report. Freeman-Sheldon syndrome (FSS) is rare, poorly understood congenital myopathic craniofacial syndrome which was first described in 1938 by Ernest Freeman, a British orthopaedic surgeon, and Joseph Sheldon, a British physician. Francis Burian independently confirmed FSS as a distinct pathological entity in 1963 and coined the striking term “whistling face” for the disease. The nomenclature of the syndrome has remained complicated since its initial description, and several synonyms encompassing its various pathognomonic features having been claimed to date. These include craniocarpo-
tarsal disease, distal arthrogyrosis Type-IIA, Whistling Face Syndrome; Whistling Face-Windmill Vane Hand Syndrome, and “Whistler” Syndrome. Recently, use of new eponym with Francis Burian’s surname (Freeman-Burian syndrome) has been suggested to replace FSS to avoid confusion with a phenotypically analogous Sheldon-Hall syndrome, though we are not sure about the awareness of the new terminology and whether it has or would replace the old one completely. The omission of some of the above information related to its nomenclature in our report on anesthetic management of two cases of FSS was purely due to the reason that the said article was not available at the time when the index report was written (towards the last quarter of 2018).

Previous authors have acknowledged that there is paucity of literature on this rare condition. The precise population prevalence of FSS remains unknown due to paucity of data and ambiguity in its diagnosis and nomenclature. A prevalence frequency of 0.9 per million is mentioned in the literature and we had mentioned it as around one in a million. Regarding its inheritance, all patterns: sporadic, autosomal dominant, and recessive types have been demonstrated but sporadic type is most reported. Allelic alterations in embryonic myosin heavy chain gene are linked with FSS. The utility of molecular testing in FSS patients as a clinical test is mainly as a research tool at present. It is a slowly progressive or non-progressive disorder as has been mentioned in several previous articles.

Diagnostic criteria for FSS at present is primarily based on pathognomonic physical findings, which include the presence of a characteristic group of craniofacial abnormalities (flat midface, small mandible and tongue, microstomia, and pursed lips accounting for a whistling face, high arched palate, prominent nasolabial folds, and H- or V-shaped chin defect). Limb deformities [ulnar deviation (90%), flexion contracture of fingers (88%) with adduction of the thumb giving the “windmill vane” appearance], kyphoscoliosis (85%), talipes equinovarus (60%) and short webbed neck are secondary and non-confirmatory findings. Cardiac involvement is possible by virtue of the primary pulmonary involvement leading to a secondary heart failure. Radiographic, muscle biopsy and electromyographic findings are typically present but not mandatory for diagnosis.

It was widely believed that up to 50% of patients with FSS are malignant hyperthermia (MH) susceptible, though this has not been corroborated in literature. Cases have been reported in the literature which report muscle rigidity, masseter spasm, and hyperpyrexia in FSS cases following halothane and succinylcholine administration, but the relation between MH and FSS has not been conclusively established so far. The myopathy in FSS patients is of myotonic type, which may be the cause of muscle rigidity seen following suxamethonium. Several FSS cases have undergone multiple uneventful anesthesics and therefore, the hyperpyrexia events may not represent true MH events and we have indicated the same in the index report. Nevertheless, it is ubiquitously accepted that the possibility of MH should be borne in mind and an MH-safe anesthetic technique is standard of care for FSS patients to date. We followed the same by avoiding succinylcholine and inhalational agents and using laryngeal mask airway on spontaneous respiration and total intravenous anesthesia (TIVA)-based technique, which is well recommended in such cases. Nonetheless, a lot of questions remain unanswered in this context and warrant further research in this area.

Opioids are an important component of balanced anaesthesia and blunt the haemodynamic changes during surgery. Fentanyl is not a long acting opioid as mentioned by the authors, rather it is a short acting opioid which is very unlikely to lead to postoperative respiratory depression in the doses mentioned in the index report especially when there was no history suggestive of preoperative respiratory involvement.

Opioid free anesthesia by use of sole regional anesthesia is an attractive alternative, but an unfeasible technique in small children. Also, use of fentanyl is preventive against emergence delirium in children. Opioids (including fentanyl and intrathecal morphine) have been used in anesthetic management of FSS in children in previous reports also without any respiratory sequelae.

There is disagreement in current literature on many clinicopathophysiologic features and anesthetic management of FSS mainly stemming from the clinical variability and rarity of the disease, and consequent lack of feasibility of randomised trials to conclusively prove many aspects.

REFERENCES


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