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Malignant Hyperthermia Syndrome

Malignant hyperthermia syndrome (MHS) is a pharmacogenetic disorder of skeletal muscle presenting as a hypermetabolic response to potent volatile anesthetic gases such as halothane, sevoflurane, desflurane, the depolarizing muscle relaxant succinylcholine and rarely after stress of vigorous exercise and heat. MHS is inherited in autosomal dominant pattern. A defect in the ryanodine receptor in chromosome 19. A receptor located in the calcium channels of the skeletal muscle sarcoplasmic reticulum. Classic signs of MHS include marked-degree hyperthermia, tachycardia, tachypnea, increased carbon dioxide production, increase oxygen consumption, acidosis, muscle rigidity and breakdown (rhabdomyolysis) and myoglobinuria. Elevations of end-carbon dioxide and temperature are the initial clues to consider MHS. MHS occur due to uncontrolled release of myoplasmic calcium which activates skeletal muscle to a hypermetabolic state causing ATP depletion, compromised muscle membrane integrity and release of potassium and rhabdomyolysis. Children comprise less than 20% of all cases. Diagnosis is established with the halothane/caffeine contracture test. Management consists of supportive measures, temperature control and Dantrolene, a specific antagonist of the pathophysiologic changes in MHS. The actual incidence of MHS has increased and the mortality is more than 15% in the Unites States. The risk of MHS in children undergoing muscle biopsy for suspected neuromuscular disease is less than 1%.

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Tumor Lysis Syndrome

Tumor lysis syndrome (TLS) refers to a group of metabolic derangements caused during abrupt and massive release of cellular components into the blood after rapid lysis of

malignant cells. This event occurs after the child receiving cytotoxic, cytolitic antibiotics or radiation therapy usually in malignancies such as leukemias, Burkitt's lymphoma and other tumors with high proliferative rate, large tumor burden or high sensitivity to chemotherapy. The release of such components and intracellular metabolites can lead to hyperuricemia, hyperkalemia, hyperphosphatemia, hypocalcemia and uremia known as TLS. The precipitation of uric acid can lead to impaired acute renal failure if not managed adequately. TLS can occur during an operation. Clinical manifestation includes nausea, vomiting, diarrhea, anorexia, lethargy, edema, fluid overload, hematuria, CHF, dysrhythmias, seizures, cramps, tetany and death. Management may consist of aggressive fluid hydration to enhance urine flow (considered the most effective strategy), alkalinization of the urine, blocking the conversion of xanthine and hypoxanthine to uric acid with allopurinol, and promoting the catabolism of uric acid with recombinant urate oxidase. Depending on risk stratification, the treatment above is instituted. Hyperphosphatemia, hyperkalemia and hypocalcemia should also be treated. The best management of TLS is prevention.

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Branchio-Oto-Renal Syndrome

The Branchio-oto-renal (BOR) syndrome is a rare autosomal dominant disorder with incomplete penetrance and extremely variable phenotypic expressivity. Main clinical features are due to congenital abnormal development of the first and second branchial arches and urinary tract. Others anomalies include early hearing impairment, preauricular pits, deformity of pinna, external auditory canal stenosis, branchial fistula and renal anomalies. Renal anomalies are always present and consist of agenesis, hypoplasia or renal dysplasia, ureteropelvic junction obstruction, vesicoureteral reflux and calyceal diverticula. There also can be bifid kidneys with double ureters and calyceal anomalies. Renal agenesia and dysplasia are the causes of end-stage renal disease in these children. Bilateral renal agenesis is the extreme, leading to a miscarriage or immediate neonatal death. The syndrome gene maps to chromosome 8q13.3 called the EYA1 gene. The BOR syndrome should be included in the differential diagnosis of deafness and chronic renal failures in children.

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