PEDIATRIC SURGERY *Update**
Volume 62 No. 03 MARCH 2024

Ovarian Dysgerminoma

Ovarian tumors are rare in children representing nearly 50% of all ovarian masses with 90% being benign. Germ cell tumors of the ovary are the most frequent histological type (60-70%) with teratoma as the main pathology. Dysgerminoma is the most common malignant germ cell tumor of the ovary representing only 2% of all ovarian cancers in children. It is most frequent during adolescence and young adulthood with a peak incidence of 15-19 years of age.

Ovarian dysgerminoma is the female counterpart of testicular seminoma derived from primitive germ cells. Dysgerminoma are often found in association with gonadal dysgenesis and abnormal ovaries that contain gonadoblastoma. Most females with ovarian dysgerminoma present with non-specific symptoms, or most commonly abdominal pain, abdominal distension, menstrual irregularity, decreased appetite, vomiting and a palpable pelvic abdominal mass. They grow rapidly, the tumor is quite large and may be associated with complications like rupture, hemoperitoneum or torsion presenting as an acute abdomen.

Though dysgerminoma are hormonally inert, a few cases have presented with precocious puberty due to elevated estradiol levels secreted by syncytiotrophoblastic giant cells and stromal luteinization. Most tumors arise from the right ovary. Dysgerminoma are bilateral in 10-15% of cases. Ovarian dysgerminoma may be associated with dysgenetic gonads that contain gonadoblastoma. Elevation of serum lactate-dehydrogenase (LDH), cancer-antigen-125 (CA-125), beta-subunit-human-chorionic-gonadotropin (B-hCG), S-100 protein, neuron-specific enolase (NSE) and placental-alkaline-phosphatase (PALP) are frequent findings in children with dysgerminoma. Alpha fetoprotein is not elevated. With elevated B-hCG pregnancy is frequently diagnosed erroneously. Pregnancy and dysgerminoma might exist together in 20-30% of cases. LDH and PALP when elevated are used as tumor markers to follow up these patients.

Diagnosis of an ovarian mass is done with CT-Scan and/or MRI. Findings are of a large well-encapsulated, multilobulated, purely or predominantly solid mass. It demonstrates an attenuation similar to muscle and nonspecific signal intensity on T2-weighted images. The characteristic imaging feature of dysgerminoma is fibrovascular septa in the tumor appearing as hypodense lines on T2-weighted images and show intense enhancement on contrast-enhanced CT and MRI images. Ovarian dysgerminoma may also contain necrosis, hemorrhage, small cystic change, or calcifications.

Grossly, dysgerminomas are typically large and solid with a homogenous creamy yellow to pink or tan and lobulated appearance. On microscopic examination the neoplasm is

characterized by delicate fibrous septa, along which are lymphocytes that intersect aggregates of polygonal clear cells with well-defined cytoplasmic borders and angulated nuclei with prominent nucleoli giving an alveolar pattern appearance. The histology is frequently referred to as "fried eggs". The presence of calcifications suggests gonadoblastoma. The finding of relatively large, round, or ovoid, "mulberry-like" calcific foci should suggest the presence of gonadoblastoma.

Most cases of ovarian dysgerminoma present as stage I. Management of dysgerminoma is primary surgical excision of the mass with unilateral salpingo-oophorectomy. Fertility sparing surgery is encouraged as frontline therapy when feasible and clinically appropriate without compromising the prognosis. The surgical approach warrants exploration of the peritoneal surface for nodules, prominent lymph node removal, omentectomy if the tumor is wrap with omentum, contralateral ovarian biopsy if abnormal and cytology of the ascitic fluid if present. Overall survival after surgery for stage I tumor is 92%.

Dysgerminoma most frequently metastasize to the peritoneal cavity, omentum (86%), pelvis, and abdomen as well as retroperitoneal lymph nodes. In higher stage dysgerminoma (FIGO stages II-IV), the guidelines recommend fertility sparing surgery followed by four cycles of chemotherapy. Dysgerminoma are radio- and chemo-sensitive. Radiotherapy is not used as frontline therapy due to the risk of secondary malignancy, premature ovarian failure, and a significant impact on future fertility.

Standard of care of management of advanced stage dysgerminoma (disease that has spread outside of the ovary) is postoperative adjuvant chemotherapy with either carboplatin or cisplatin combined with etoposide and Bleomycin. Cisplatin based therapy is associated cardiovascular disease, development of secondary malignant neoplasm in survivors, ototoxicity, nephrotoxicity and gonadotoxicity (premature ovarian failure). Patients with advanced stage dysgerminoma have an excellent five-years event free survival and overall survival across all age groups with both cisplatin and carboplatin therapy. Clinical trial data support the use of carboplatin-based therapy with or without Bleomycin as frontline treatment for all patients with advanced stage dysgerminoma to minimize treatment-related toxicity without significantly compromising therapeutic efficacy.

References:

1- Shah R, Xia C, Krailo M, et al: Is carboplatin-based chemotherapy as effective as cisplatin-based chemotherapy in the treatment of advanced-stage dysgerminoma in children, adolescents and young adults? Gynecol Oncol. 150(2):253-260, 2018

2- Zhao S, Sun F, Bao L, et al: Pure dysgerminoma of the ovary: CT and MRI features with pathological correlation in 13 tumors. J Ovarian Res. 13(1):71, 2020

3- Warnnissorn M, Watkins JC, Young RH: Dysgerminoma of the Ovary: An Analysis of 140 Cases Emphasizing Unusual Microscopic Findings and Resultant Diagnostic Problems. Am J Surg Pathol. 45(8):1009-1027, 2021

4- Maidarti M, Garinasih PD, Anggraeni TD: Conservative surgical staging as a means to preserve fertility in patients with dysgerminoma: a case report. Ann Med Surg (Lond). 85(3):427-430, 2023

5- Adhikari S, Joti S, Chhetri PK: Paediatric Ovarian Dysgerminoma: A Case Report. JNMA J Nepal Med Assoc. 60(255):985-988, 2022

6- Wood GE, Bunting CP, Veli M, et al: Seminoma and dysgerminoma: evidence for alignment of clinical trials and de-escalation of systemic chemotherapy. Front Oncol. 13:1271647, 2023

7- Birbas E, Kanavos T, Gkrozou F, Skentou C, Daniilidis A, Vatopoulou A: Ovarian Masses in Children and Adolescents: A Review of the Literature with Emphasis on the Diagnostic Approach. Children (Basel). 10(7):1114, 2023

Pouch Failure

Children with ulcerative colitis, familial adenomatous polyposis, and total colonic aganglionosis benefit from ileal pouch-anal anastomosis (IPAA) as a standard restorative procedure. Most of these reconstructed ileoanal pouches report a good quality of life with excellent outcomes. However, a significant number of patients develop short- and long-term complications such as anastomotic leak or stricture, fistula, pelvic sepsis, recurring pouchitis, the development of perianal Crohn's disease, and pouch dysfunction.

Complications can lead to pouch failure, which has been reported to occur in up to 15% of all patients (5-15%). Pouch failure is defined as the need for pouch resection, permanent diversion, or a revision/redo of the pouch procedure. The most common causes of pouch failure include pelvic sepsis, poor pouch function, pouchitis, and de novo Crohn's disease. Patients who develop perineal Crohn's have the highest rate of pouch failure (47%), and the distribution of pouch failure does not show significant gender differences.

Complications leading to pouch failure can occur either early (26%) or late (76%). In early failures, pelvic sepsis due to anastomotic complications (bleeding, stapler malfunction, ischemia, tension) plays a major role, and anastomotic leakage is an independent risk factor for pouch failure. In late pouch failures, pouch-related fistulas with chronic sinus formation play a major role. Primary sclerosing cholangitis associated with ulcerative colitis can increase pouchitis rates as well as the risk of postoperative sepsis.

Patients with pouch dysfunction present with a significant decrease in their quality of life, reporting symptoms such as bowel movements of more than 20 times per day, urgency, tenesmus, draining fistulas, hematochezia, and abdominal pelvic pain. These symptoms can lead to food, work, and sexual restrictions, causing psychological impairments and general debilitation.

Once pouch failure ensues, the child has several alternatives: reconstructing the pouch, permanent ileostomy with pouch excision, or leaving the pouch in situ. Redo pouch surgery is lengthy and complex, with an overall morbidity rate of 40% after salvage pouch surgery. Complications of redo surgery include pouch fistula, stricture, pelvic abscess, and pouch-vaginal fistula, with higher rates in those who had pouch excision with the creation of a new pouch compared to those whose old pouch was utilized. Bowel incontinence after redo surgery is also higher.

Pouch failure is significantly associated with Crohn's disease-like pouch inflammation, biologic use, and pouch revision. Pouch excision with permanent ileostomy is a complex procedure due to the need for reoperation within the pelvis, posing a risk of damage to pelvic structures and septic complications. Leaving the pouch in situ may lead to symptoms of seepage from the anal canal and the potential risk of harboring cancer in the pouch.

Permanent ileostomy is considered an alternative option when pouch excision may not be feasible or advisable. Patients with incontinence, outlet obstruction, or fistula are better served by pouch excision because they continue to experience troubling anal symptoms after leaving the pouch in situ. Sexual function is better maintained after leaving the pouch in place than after pouch excision.

In general, pouch excision with permanent diversion is the treatment of choice for patients with pouch failure, associated with improved quality of life and prevention of perineal symptoms, including anal pain and seepage. Leaving the pouch in situ is an option when concern about reoperation in the pelvis could cause significant urinary and sexual complications. The long-term risk of developing dysplasia in the retained pouch seems to be minimal, although pouch endoscopic surveillance should be performed for the early detection of any silent neoplastic transformation of the pouch or residual anorectum.

References:

1- Kiran RP, Kirat HT, Rottoli M, Xhaja X, Remzi FH, Fazio VW: Permanent Ostomy After ileoanal pouch Failure: Pouch in Situ or Pouch Excision? Dis Colon Rectum 55:4-9, 2012
2- Pappou EP, Kiran RP: The Failed J Pouch. Clin Colon Rectal Surg. 29(2):123-9, 2016
3- Helavirta I, Lehto K, Huhtala H, Hyoty M, Collin P, Aitola P: Pouch failures following restorative proctocolectomy in ulcerative colitis. Int J Colorectal Dis. 35: 2027-2033, 2020
4- Heuthorst L, Wasmann KATGM, Reijntjes MA, Hompes R, Buskens CJ, Bemelman WA: Ileal Pouch-anal Anastomosis Complications and Pouch Failure: A systematic review and meta-analysis. Ann Surg Open. 2021 2(2):e074, 2021
5- Alsafi Z, Snell A, Segal JP: Prevalence of 'pouch failure' of the ileoanal pouch in ulcerative colitis: a systematic review and meta-analysis. Int J Colorectal Dis. 37(2):357-364, 2022
6- Lynn PB, Brandstetter S, Schwartzberg DM: Pelvic Pouch Failure: Treatment Options. Clin Colon Rectal Surg. 35(6):487-494, 2022

Refeeding Syndrome

Refeeding syndrome (RS) is an acute metabolic disturbance and potentially life-threatening condition that occurs upon the sudden and rapid reintroduction of oral, enteral, or parenteral nutrition after prolonged fasting or suboptimal feeding. This disease is characterized by a rapid shift in electrolyte and fluid balance that can cause a range of symptoms and complications, including cardiac arrhythmia, shortness of breath, seizures, and even death.

The body undergoes a transition from a catabolic to an anabolic state during refeeding. This shift creates an intracellular demand for metabolites such as inorganic phosphorus (P), potassium (K), magnesium (Mg), and thiamine (Vitamin B1), leading to a deficient state resulting in hypophosphatemia, hypokalemia, and hypomagnesemia.

Re-eating, especially carbohydrates, raises insulin levels, promoting glucose uptake and utilization by cells. This process results in rapid changes in electrolytes and fluid balance, as potassium, magnesium, and phosphate enter the cells, causing a reduction in these electrolyte levels in the blood.

RS in adolescents and young adults is commonly associated with marked malnutrition,

particularly in cases of anorexia nervosa. Other children at risk include those with celiac disease, cancer, cerebral palsy, congenital heart or lung disease, postoperative status, and Crohn's disease.

RS can manifest clinically as a mild electrolyte disturbance without significant symptoms or as a severe electrolyte disorder leading to severe organ failure, such as respiratory and cardiac failure, cardiac arrhythmias, seizures, muscle weakness, horizontal nystagmus, and encephalopathy (Wernicke's). The mortality after developing RS can be as high as 70%.

Children at high risk for developing RS include those with significantly reduced energy intake for up to ten days before the reintroduction of nutrition, as well as those who are malnourished. Patients in the pediatric intensive care unit (PICU) are at risk of developing RS at the time of feeding, with the incidence increasing with the duration of PICU stay.

To establish the diagnosis of RS, the American Society for Parenteral and Enteral Nutrition has outlined criteria involving a decrease in serum phosphorus, potassium, or magnesium levels by a certain percentage, and/or organ dysfunction resulting from these changes within five days of reinitiating or substantially increasing energy provision.

The incidence of RS among critically ill children at risk is high (46%) and severe most of the time. The PICU length of stay and acquired infections were higher in children who developed RS than in those at risk who did not.

Main management strategies for RS in children involve a multidisciplinary approach with careful monitoring and supportive care to prevent and treat the complications of this condition. Management of eating disorders, such as anorexia nervosa in adolescents and young adults, consists of the gradual restoration of weight and the prevention or treatment of clinical complications.

Despite this, there is no clear consensus in management. Refeeding should start at a low level of energy replacement with vitamin supplementation initiated during refeeding and continued for at least 5-7 days. Correction of fluid and electrolyte imbalances prior to feeding is not necessary and should be done simultaneously. Prevention of RS requires small amounts of low-calorie fluids, checking electrolytes, and thiamine supplementation. This can be achieved by gradually increasing the number of calories in the diet and monitoring potassium, magnesium, and phosphate.

RS is a serious condition that can be managed with careful monitoring and controlled treatment.

References:

1- Runde J, Sentongo T: Refeeding Syndrome. Pediatr Ann. 48(11):e448-e454, 2019

2- da Silva JSV, Seres DS, Sabino K, et al: ASPEN Consensus Recommendations for Refeeding Syndrome. Nutr Clin Pract. 35(2):178-195, 2020

3- Blanc S, Vasileva T, Tume LN, et al: Incidence of Refeeding Syndrome in Critically Ill Children With Nutritional Support. Front Pediatr. 2022 Jun 21;10:932290. doi: 10.3389/fped.2022.932290. eCollection 2022.

4- Corsello A, Trovato CM, Dipasquale V, et al: Refeeding Syndrome in Pediatric Age, An Unknown Disease: A Narrative Review. J Pediatr Gastroenterol Nutr. 2023 Dec 1;77(6):e75-e83. doi: 10.1097/MPG.0000000000003945. Epub 2023 Sep 14.

***Edited by: Humberto Lugo-Vicente, MD, FACS, FAAP**
Professor of Pediatric Surgery, UPR - School of Medicine, UCC School of Medicine & Ponce School of Medicine.
Pediatric Surgery, San Jorge Children's & Woman Hospital.
Postal Address: P.O. Box 10426, San Juan, Puerto Rico USA 00922-0426.
Tel (787) 340-1868 E-mail: *pediatricsurgerypr@gmail.net*
Internet: pedsurgeryupdate.com

**** PSU 1993-2024***
ISSN 1089-7739