Vol 1| Issue 3 | 2022

Pedia Companion

Pedia Companion Newsletter
Vol 1 | Issue 3 | 2022

Dear Doctor,
Greetings from Micro Labs Limited. We are happy to bring you "PEDIA COMPANION" which contain latest and interesting news in the field of Paediatrics.

This issue contain:

1. **The challenges of managing incisional hernia in children and infants**
2. **Effect of fetal growth restriction on brain volume and white matter microstructure in children at the early school age**
3. **Wheeze is an inconsistent outcome for bronchial methacholine challenges.**
4. **Translocation-associated Perivascular Epithelioid Cell Neoplasm (PEComa) in a 17-year old adolescent**

Looking forward to your valuable feedback

Best Regards,
Medical Team, Micro Labs Limited

Vol 1| Issue 3 | 2022

Pedia Companion

1. The challenges of managing incisional hernia in children and infants

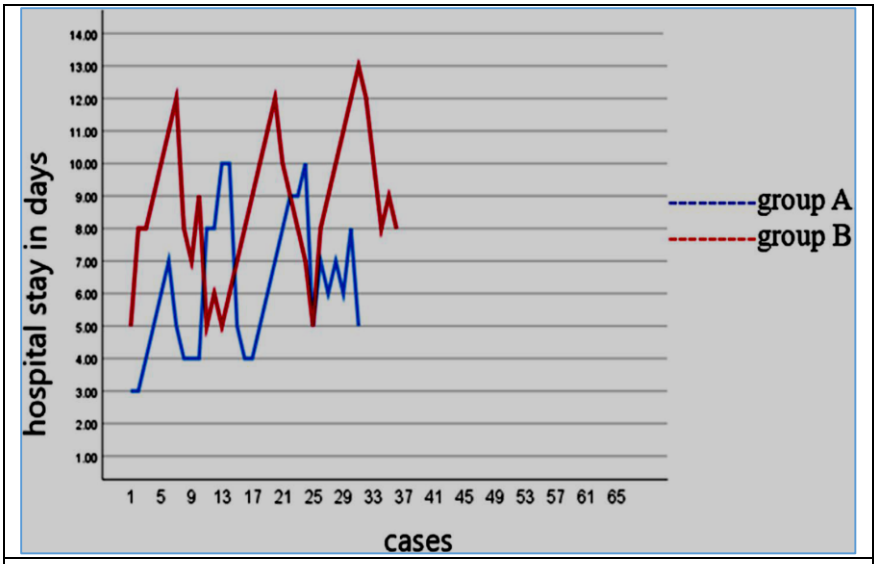
Introduction:

One of the most common postoperative consequences of open and laparoscopic surgery is incisional hernia (IH). IH might cause edoema, intestinal blockage, or skin irritation issues.[1]According to certain research, the incidence of incisional hernia in children and infants (IHCI) varied from 1% to 3% of all operated patients. The lack of detection of several new born disorders such as necrotizing entero-colitis (NEC) and infantile hypertrophic pyloric stenosis (IHPS) was a drawback of these findings. Furthermore, the existence of a stoma was shown to be strongly linked to an elevated risk of IHCI. The factors that contribute to the development of incisional hernia have been thoroughly studied in adults, but not in paediatric patients.[2] As a result, researchers wanted to evaluate the challenges related with the incidence, treatment, and prognosis of IHCI patients treated at a tertiary level hospital.

Children and infants with Incisional hernia will be in the hospital for an extended period of time and may require ventilatory support during their postoperative period.

Methods:

This is a retrospective study of all children and infants who had an incisional hernia after having an elective or urgent laparotomy. Patients were divided into two groups based on their age: group A comprised of infants with incisional hernia under the age of two years, and group B included children older than two years. A swelling at the incision site, persistent colicky abdominal pain, or the clinical image of a complex hernia were the presenting symptoms. The age at primary surgery, gender, prematurity, the indication for surgery, the general condition of the patients, nutritional status, the presence of a surgical site infection, the onset of incisional hernia, the presenting symptoms, the size of the defect, the type of repair, the mean duration of postoperative ventilation if needed, the occurrence of any complications, the mean hospital stay, and the onset of the rectal hernia were the variables examined.



The duration of the hospital stay per patient in both groups

Results:

All infants and children with incisional hernia were included in a retrospective analysis. Patients were divided into two groups based on their age at the time of presentation: group A Children under the age of two and group B patients above the age of two. In customised charts, all data from the initial operation, as well as data from the incisional hernia repair, were collected. There were 67 patients in the trial. In group A, the median age was 6.5 months, whereas in group B, it was 10.5 years. In group A, 35.4 % of patients had urgent presentation, compared to 19.44 % in group B. In 64.5 % of instances in group A and 52.7 % of cases in group B, tissue repair was employed as the final treatment.

Discussion:

The researchers' expertise managing IHCI in a tertiary-level hospital was highlighted in this study. Only a few papers in paediatrics addressed this issue. For parents, patients, and paediatric surgeons, it is a painful and difficult scenario. Several causes have contributed to the emergence of this problem. The occurrence of IHCI is one of them. Because of two factors, determining the incidence is challenging. The first is attributable to an increase in the incidence of IHCI when the follow-up time is extended. The second is because there is a chance that the defect will spontaneously resolve and close with follow-up. One out of every seven cases of IHCI resulted in spontaneous disappearance, which was more common in patients who had their first surgery while in neonatal age.[2] Schattenkerk et al. concluded in their retrospective research that the site of the incision, the suture material, the closure method, and the suturing technique had no significant influence on the development of incisional hernia in infant's expectation.[3]

Conclusion:

Incisional hernia is a complicated complication that can present itself in a number of different ways. Every patient's treatment is tailored to their specific needs. If the defect is more than 4 cm in maximum width, a mesh repair is advised. These children and newborns will be in the hospital for a long time and may require ventilatory assistance in the early stages of their recovery.

References:

1. Tanaka K, Misawa T, Ashizuka S, Yoshizawa J, Akiba T, Ohki T. Risk Factors for Incisional Hernia in Children. World J Surg. 2018 Jul;42(7):2265-2268.
2. Khirallah, M.G., Elkhadrawy, O.H., Eldessouki, N.E. *et al.* The challenges of the management of the incisional hernia in children and infants: a retrospective experience of a tertiary hospital. *Ann Pediatr Surg* **18,** 20 (2022).
3. Eeftinck Schattenkerk LD, Musters GD, Coultre SEL, de Jonge WJ, van Heurn LE, Derikx JP. Incisional hernia after abdominal surgery in infants: A retrospective analysis of incidence and risk factors. J Pediatr Surg. 2021 Nov;56(11):2107-2112.

Vol 1| Issue 3 | 2022

Pedia Companion

2. Effect of fetal growth restriction on brain volume and white matter microstructure in children at the early school age

Introduction:

Placental insufficiency is the most prevalent cause of foetal growth restriction, which affects 5%–10% of all pregnancies.[1] Impaired placental blood flow causes persistent foetal hypoxia and malnutrition, as well as blood flow redistribution to key foetal organs, the heart, and the brain. Short and long-term outcomes like distinct profile of neurocognitive impairments, including speech, language, and literacy challenges are influenced by placental and foetal haemodynamic alterations, and infants born with foetal growth restriction have difficulty with neurocognitive processing from infancy to adulthood, even if there is no particular perinatal brain injury.[1,2] The objective of this study was to see how prenatal growth restriction and foetal haemodynamic disorders affect brain sizes and white matter microstructure in children at the early school age.

Significant alterations in white matter microstructure were seen in children aged 8–10 years' old who were born with foetal growth restriction, but no variations in grey and white matter volumes were found.

Methods:

This study conducted by *Korkalainen et al.* looked at 32 children born with foetal growth restriction between the ages of 24 and 40 weeks of pregnancy, as well as 27 gestational age-matched children. At the age of 8–10 years, all of the children had magnetic resonance imaging (MRI). For brain MRI, an 8-channel head coil was employed. During scanning, the child's head was covered by soft cushions, and ear plugs were employed to shield the child from the imaging noise. On 17 children born with foetal growth restriction and 14 children born with birth weight acceptable for gestational age, cerebral volumes were measured, and tract-based spatial statistics and atlas-based white matter analyses were done. Atlas-based studies were done to supplement the whole-brain tract-based spatial statistics analyses, utilising ROIs from the JHU ICBM-DTI-81 (Johns Hopkins University, International Consortium for Brain Mapping) white-matter probabilistic tractography atlas provided in the FSL package.

Results:

The total intracranial volumes of children born with foetal growth limitation were less than those of children born with normal foetal development, but no significant variations in grey or white matter volumes were found (Table 1). When comparing children born with foetal growth restriction to children born with normal foetal development, atlas-based white matter analysis revealed greater mean and radial diffusivity values in large white matter tracts.

Discussion:

In this study, 8–10-year-old children who were born with foetal growth restriction at 24–40 gestational weeks had smaller total intracranial volumes than their mates who had normal foetal development, with no change in grey and white matter volumes. However, a more detailed atlas-based analysis revealed differences in white matter tracts across the compared groups,

suggesting differences in white matter maturation at early school age. In a cohort of 7-year-old infants born very preterms. The overall brain volume of children with NDI was lower, and the microstructure of three main white matter pathways was different in those with neurodevelopmental impairment had changed brain anatomy compared to those without neurodevelopmental impairment in a cohort of 7-year-old infants born very preterms is comparable to this study finding.[3] Researchers believe that the discrepancies between our tract-based spatial statistics and atlas-based analyses and earlier findings in the literature are partially attributable to the ROI method's better statistical power when compared to voxel-wise methodologies.[4]

Volume (cm^3 [SD])	FGR ($n=32$)	FGR UA PI > 2 SD ($n=22$)	FGR CPR <-2 SD ($n=16$)	AGA ($n=27$)
Total intracranial volume	1,382[a]	1,375[b]	1,384	1,452
	(152)	(130)	(155)	(93)
Grey matter	746	741	744	770
	(60)	(54)	(60)	(51)
White matter	427	425	422	442
	(52)	(44)	(51)	(43)
Cerebrospinal fluid	209	208	218	240
	(64)	(64)	(72)	(61)

Cerebral tissue volumes (cm3) at the age of 8–10 years in children born with fetal growth restriction (FGR), FGR children with prenatally detected significant placental insufficiency (umbilical artery pulsatility index [UA PI] > 2 standard deviations [SD]), FGR children with prenatal cerebral redistribution (cerebroplacental ratio [CPR] < -2 SD) and in children with appropriate growth for gestational age (AGA). The values given are mean (± standard deviation [SD])

Conclusion:

The study concludes that even though no abnormalities in grey and white white matter volumes were found, children aged 8–10 years old born with foetal growth restriction showed substantial alterations in white matter microstructure when compared to children of the normal gestational age. White matter maturation can be hampered by poor foetal growth, which can lead to neurodevelopmental problems in future.

References:

1. Korkalainen N, Ilvesmäki T, Parkkola R, Perhomaa M, Mäkikallio K. Brain volumes and white matter microstructure in 8- to 10-year-old children born with fetal growth restriction. Pediatr Radiol. 2022 Apr 22.
2. Korkalainen N, Partanen L, Räsänen J, Yliherva A, Mäkikallio K. Fetal hemodynamics and language skills in primary school-aged children with fetal growth restriction: A longitudinal study. Early Hum Dev. 2019 Jul;134:34-40.
3. Kennedy E, Poppe T, Tottman A, Harding J. Neurodevelopmental impairment is associated with altered white matter development in a cohort of school-aged children born very preterm. Neuroimage Clin. 2021;31:102730.
4. Hunter LE, Lubin N, Glassman NR, Xue X, Spira M, Lipton ML. Comparing Region of Interest versus Voxel-Wise Diffusion Tensor Imaging Analytic Methods in Mild and Moderate Traumatic Brain Injury: A Systematic Review and Meta-Analysis. J Neurotrauma. 2019 Apr 15;36(8):1222-1230

Vol 1| Issue 3 | 2022

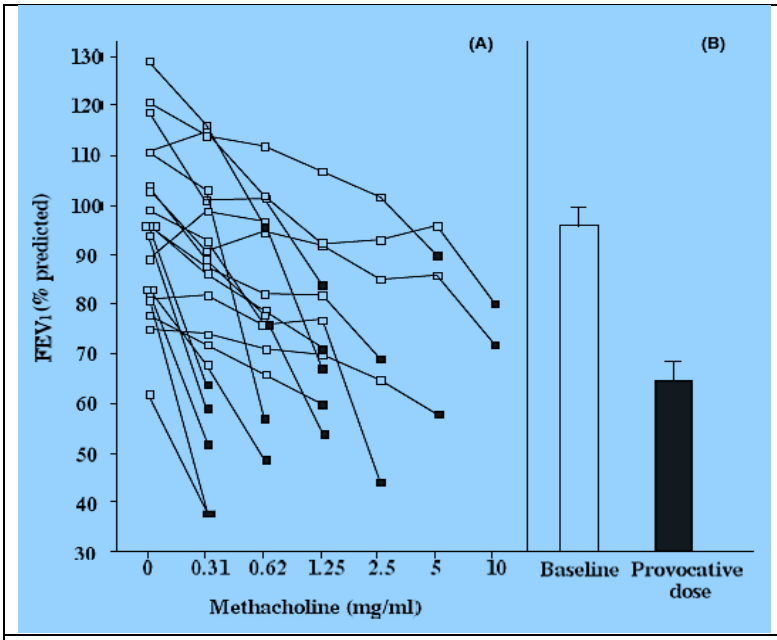
Pedia Companion

3.Wheeze is an inconsistent outcome for bronchial methacholine challenges.

Introduction

Bronchial hyper responsiveness (BHR) is a common 'hallmark' of asthma, and broncho-provocation testing is routinely used to confirm a diagnosis. BHR has been found as a key predictor of wheezing severity and persistence in later childhood.[1] The gold standard testing for determining BHR is bronchial provocation challenges, but there is no universally recognised endpoint for determining a positive challenge in young children who cannot perform spirometry, as there is for older children and adults who use PC20 FEV1 (provocative concentration of methacholine causing a 20% drop in FEV1-forced expiratory volume in one second)..[2] Previous studies has suggested that the presence of wheezing by auscultation, or the so-called $_{PCwheeze}$, can indicate a positive bronchial challenge in children who are unable to conduct spirometry. The current measures used to assess BHR in young children with suspected asthma result in a larger degree of respiratory impairment than older children performing an MCh challenge using the PC20 FEV1.[1] To address this issue, researchers conducted a prospective study in which the physical examination findings and SpO2 of preschool children who had a positive MCh challenge were compared to those of older children who had a positive MCh challenge and spirometry.

wheezing is an uncommon physical finding in young children, despite several other physical findings that imply a favourable Methacholine challenge



A) Serial FEV1 values for each school-aged subject during the methacholine challenge. Open squares represent FEV1 values at each methacholine dose prior to a fall in FEV1 of ≥20%, while closed squares represent the FEV1 values at the time of a positive methacholine challenge. (B) Mean FEV1 values at baseline and at the time of a positive methacholine challenge. Data are presented as mean ± SEM

Methods:

This was a prospective research study conducted by *Stewart et al*. Patients aged 1 to 17 years old were eligible to participate in the trial. Patients aged 1–5 years old in the preschool group had a history of recurrent respiratory symptoms and at least one recorded episode of wheezing. Before the challenge, all subjects abstained from taking short-

acting bronchodilators for at least 8 hours and long-acting bronchodilators for at least 24 hours. A 2-minute tidal breathing method was used in the MCh challenge, with a low-output nebulizer and a facemask or mouthpiece. The nebulizer was driven by compressed air at a rate of 5 L/min. Starting with a placebo, nebulized treatments were administered over 2 minutes via mask or mouthpiece, with each doubling-concentration of MCh. Positive BCT was defined as either persistent cough, wheeze, a 5% drop in oxygen saturation (SpO2), or a 50% increase in respiratory rate (RR) from baseline in preschool children (n = 22), and the concentration of methacholine (MCh) required to elicit a 20% decline in FEV1 in school-aged children (n = 22). (PC20).

Results:

A positive BCT was found in all preschool children (mean age 3.4 years) (median provocative MCh concentration 1.25 mg/ml [IQR, 0.62, 1.25]). A positive BCT was found in twenty (91%) school-aged children (mean age 11.3 years) (median PC20 1.25 mg/ml [IQR, 0.55, 2.5]). The mean drop in SpO2 (6.9% vs. 3.8%) and the mean percent increase in RR (61 % vs. 22 %; p =.001) were higher in preschool-aged children than in school-aged children at the time of the positive BCT. A small percentage of children developed wheezing after receiving a positive BCT (23 % preschool vs. 15% school-aged children; p =0.5).s

Discussion:

In contrast to previous research, researchers discovered that wheezing during a positive MCh challenge was a rare occurrence, appearing in less than 25%. Despite the absence of wheezing, the pre-schoolers exhibited considerable respiratory impairment, as seen by an increase in RR, retractions, and hypoxemia.[3] Only 8 of the 40 participants investigated (20%) would have been regarded to have a positive MCh challenge if wheezing had been the primary endpoint, hence the findings are of great clinical significance. Researchers would have compared changes in lung function to other indicators in preschool-aged children, such as oxygen saturation and auscultation for the presence of wheeze. Unfortunately, there is no gold-standard lung function manoeuvre for preschoolers, particularly those aged 2–4.[2] Although young children can perform impulse oscillometry, which can detect changes in respiratory system properties and reflect peripheral airway obstruction, only 50% of 3-year-olds can do so consistently and reliably, making it an unsatisfactory test compared to spirometry when serial measurements are required, such as when completing an MCh challenge. Furthermore, impulse oscillometry has less standardisation as a method of measuring the response to bronchial stressors.

Conclusion:

In conclusion, wheezing is an uncommon physical finding in young children, despite several other physical findings that imply a favourable MCh challenge. Endpoints such as a 3% decline in SpO2 or a 25% increase in respiratory rate, according to the researchers, would be sufficient to detect the presence of BHR in young children who are unable to complete spirometry, as these endpoints would have detected all of the positive MCh challenge findings. while avoiding unnecessarily aggravated respiratory distress

References:

1. Stewart L, Miyazawa N, Covar R, Mjaanes C, Shimamoto R, Gleason M, Peroni D, Spahn JD, Comberiati P. Wheeze is an unreliable endpoint for bronchial methacholine challenges in preschool children. Pediatric Allergy and Immunology. 2022 Apr;33(4):e13767.

2. Comberiati P, Katial RK, Covar RA. Bronchoprovocation testing in asthma: an update. Immunology and Allergy Clinics. 2018 Nov 1;38(4):545-71.
3. Caussade S, Castro-Rodriguez JA, Contreras S, Bugueño R, Ramirez R, Padilla O, Einisman H, Holmgren et al. Methacholine challenge test by wheezing and oxygen saturation in preschool children with asthma. Allergologia et Immunopathologia. 2015 Mar 1;43(2):174-9.
4. Kattan M, Bacharier LB, O'Connor GT, Cohen R, Sorkness RL, Morgan W et al. Spirometry and impulse oscillometry in preschool children: acceptability and relationship to maternal smoking in pregnancy. The Journal of Allergy and Clinical Immunology: In Practice. 2018 Sep 1;6(5):1596-603.

4.Translocation-associated Perivascular Epithelioid Cell Neoplasm (PEComa) in a 17-year old adolescent.

Introduction:

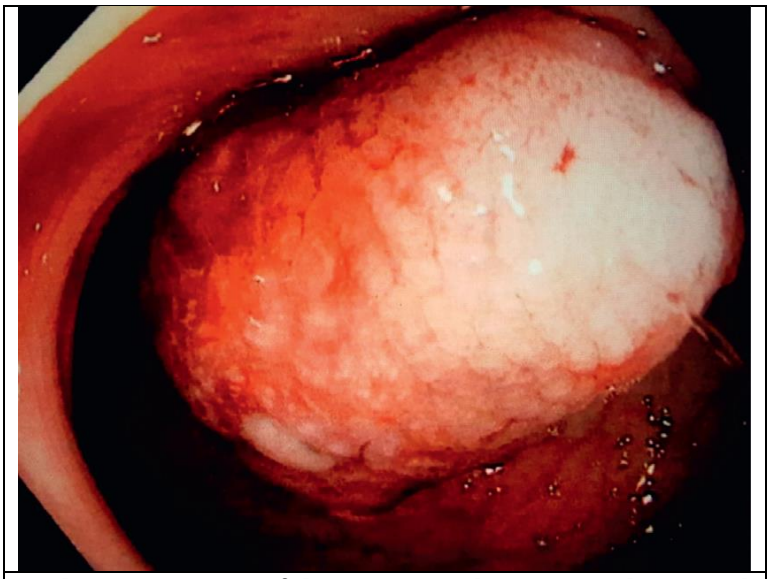
A gastrointestinal polyp is a tumour that extends into the digestive tract lumen from a mucous membrane. One of the most prevalent indications of a paediatric colorectal polyp is hematochezia, passing of fresh blood in anus or with faeces. PEComa is a rare mesenchymal tumour made up of perivascular epithelioid cells that has unique histological, immunohistochemical, and genetic characteristics.[1] Gastrointestinal PEComas are extremely uncommon in children.[2] Here is a case of 17-year-old male presented with hematochezia, abdominal pain, and anaemia. A polypoid tumour in the sigmoid colon was discovered during an endoscopy. PEComa was verified by histological and immunochemical examinations. TFE3-SFPQ rearrangement owing to translocation resulted in an in-frame fusion of TFE3 exons 1–4 to SFPQ exons 8–10, according to molecular study employing next-generation DNA-sequencing technology. Although TFE3-SFPQ fusion translocation is frequent in PEComas, this translocation has never been documented in GI PEComas.

This case report provides insight into this rare entity as well asdiscusses the pathophysiological aspects of TFE3-SFPQ-associated GI Perivascular Epithelioid Cell Neoplasm (PEComa)

Case Presentation:

For one week, a 17-year-old male had abdominal pain and bloody stools. Patient's faeces were well-formed, with bright red blood, but patient began to experience greater frequency and urgency of defecation, as well as melena, over the course of the week. Abdomen pain was widespread, intermittent, and colicky, and defection did not reduce it. Patient He had a significant medical history of moderate chronic asthma that was adequately treated with inhaled corticosteroids. Patient suffered dyspepsia a few years ago as a result of candida esophagitis. haemoglobin level of 14 mg/dl the day before the presentation, a computed tomography (CT) abdomen with oral contrast was normal, and stool cultures were negative. A repeat CBC revealed a haemoglobin level of 12.2 mg/dl, no leukocytosis, but a slightly raised C-reactive protein (CRP) level of 25 mg/L (normal 7 mg/L). Patient's abdomen pain improved after receiving an intravenous H2 receptor antagonist, but a repeat CBC indicated a further drop in haemoglobin to 10.7 mg/dl the next day. An esophagogastroduodenoscopy revealed no signs of bleeding or a cause of it. During a colonoscopy, a single large bleeding pedunculated sigmoid polyp measuring 2 cm*1.5 cm*1.5 cm was discovered . The mass was removed

endoscopically and submitted for histological analysis. The lymph nodes were examined and confirmed to be benign, thus they were not sent for pathological examination. Pathological and microscopic analysis of the sigmoid colon sample revealed a polypoid mass with a stalk length 2.0 *1.5* 1.3 cm. Lesional cells involving the colonic mucosa and submucosa were found to have a nested pattern with clear to eosinophilic granular cytoplasm, well-defined cell boundaries, and round nuclei with prominent nucleoli. the resection margins were clear of lesional cells and measured 0.5 cm away from them. The HMB-45 and TFE3 immunohistochemical stains were positive. the diagnosis of TEF3 rearranged PEComa was made based on the tumour morphology and staining pattern. The formalin-fixed tumour cells were subjected to next-generation DNA-sequencing technology-based mutational investigation utilising the MSK-IMPACTassay. The TFE3-SFPQ rearrangement was demonstrated in the test owing to translocation caused by an in-frame fusion of TFE3 exons 1–4 with SFPQ exons 8–10. There were no additional major mutation changes found. The MSI sensor score for microsatellite instability was 0.1, confirming MSI stability. Biopsies obtained during upper endoscopy and colonoscopy were all normal. Abdominal CT scan of the abdomen found no signs of metastases.



Endoscopic image of the PEComa showing a submucosal polypoid mass with surface ulceration located in the sigmoid colon.

Discussion:

PEComas of the GI tract appear to have a wide spectrum of biological activity, ranging from benign tumours to aggressive high-grade sarcomas that can spread despite TFE rearrangement. The most effective medicines in the treatment of patients with advanced/metastatic PEComa are mTOR inhibitors. Further , antiangiogenics and chemotherapy with gemcitabine- or anthracycline-based regimens are alternatives, but with a decreased response rate.[3] A 31-year-old woman with malignant GI PEComa that had spread to her liver was found to have a TFE3-SFPQ rearrangement in one case report. TSC and non-TSC linked high-grade PEComas are usually treated with a combination of mTOR inhibitors and exemestane, however the tumour in this case was only responsive to anti-VEGFR TKI Apatinib treatment.[4] Overall, more studies on the genetic precursor and molecular activity of GI and non-GI PEComas are necessary to understand the clinical course and biological behavior. the tumor cells in this patient demonstrated an in-frame fusion of TFE3 exons 1–4 to SFPQ exons 8–10, which has never been reported in a GI PEComas.[1]

s

Conclusion:

Researchers conclude that this case report sheds light on this uncommon condition and explores previously unknown pathophysiological elements of TFE3-SFPQ fusion-associated GI PEComas.

References:

1. Pereira K, Inamdar AA, Zaveri A, Teitelbaum JE, Shertz W, Belitsis K. A Rare Case of a Translocation-Associated Perivascular Epithelioid Cell Neoplasm (PEComa). Case Rep Pediatr. 2022 Apr 21;2022:7519456.
2. Baba, T., Kawano, T., Saito, Y. *et al.* Malignant perivascular epithelioid cell neoplasm in the liver: report of a pediatric case. *surg case rep* **7,** 212 (2021).
3. Sanfilippo R, Jones RL, Blay JY, Le Cesne A, Provenzano S, Antoniou G et al. Role of chemotherapy, VEGFR inhibitors, and mTOR inhibitors in advanced perivascular epithelioid cell tumors (PEComas). Clinical Cancer Research. 2019 Sep 1;25(17):5295-300.
4. Xu J, Gong XL, Wu H, Zhao L. Case Report: Gastrointestinal PEComa With TFE3 Rearrangement Treated With Anti-VEGFR TKI Apatinib. Frontiers in Oncology. 2020 Nov 23;10:2587.