SPEAK

The Voice Of PEAK

The official newsletter of

Paediatric Endocrinology Association of Karnataka

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The Office Bearers Speak

It gives us great pleasure to introduce the second issue of our very own newsletter SPEAK. As we know Speak is the voice of Paediatric Endocrinology Association of Karnataka. I would like to congratulate the entire team of PEAK for going above and beyond in creating awareness in the field of Paediatric Endocrinology through conferences, activities and continued medical education. I would also like to wish the team the best of luck for the prep of the massive upcoming event in November 2023 -the Biennial ISPAE conference at Bengaluru. This way, we shall continue to create abundant awareness in the field of Paediatric Endocrinology among all medical practitioners, students, nurses and parents at grass root level.

Happy learning!

Warm regards

Shaila Bhattacharyya
President PEAK

Raghupathy Palany
Chief Advisor PEAK

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HELLO FROM THE EDITORIAL BOARD

Dear All

It gives us great pleasure in creating a continuum and launching the second issue our newsletter-**SPEAK**.

This newsletter shall highlight all the efforts put in by the PEAK members in sensitizing the Paediatricians, students, clinicians and parents of the children with Paediatric Endocrine disorders.

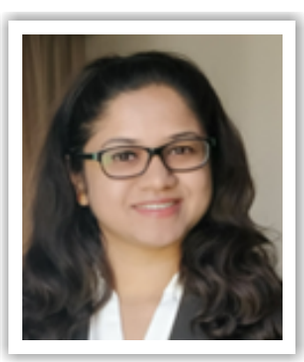
Our cover page is innovatively designed by the art of our little wonders (our patients). Going through this newsletter shall pleasantly walk you through interesting case reports, multiple events and programs conducted and drug reviews.

We wish to see more members come along in our journey of creating massive awareness in Paediatric Endocrinology and contributions from the members in the upcoming issues

Wishing you all a memorable experience and hope to see the same enthusiasm in the upcoming issues as well.

Thank you!

Vijaya Sarathi H.A.
Editor



Diksha Shirodkar
Co-editor

A WARM WELCOME TO OUR NEW MEMBERS

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- **Anshika Singh**
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  Fellow Paediatric Endocrinoogy, Manipal Hospital, Bangalore, Karnataka

Activities by PEAK Members

The CME programs under the flagship of PEAK

The CME programs under the flagship of PEAK

Growth and Puberty- A Challenging Journey

Dr Suman Rath (Local Co-ordinator)Bangalore Baptist Hospital

A Pediatric Endocrine Workshop was organized in Bangalore Baptist Hospital under the banner of IAP-BPS in association with PEAK on 06/11/2022.

The workshop was attended by 45 delegates , 6 faculty and 3 IAP Bangalore dignitaries. The workshop started with short prayer and the 1st session was by Dr Poornima on Growth monitoring of children .It was followed by Approach to Short Stature by Dr Shaila Bhattacharyya. Dr Pavitra took the 3rd session related to vitamin D deficiency and Rickets. It was followed by a short Inauguration wherein dignitaries like Senior Paediatric Endocrinologist and Chief advisor of PEAK Dr P Raghupathy, President elect IAP Bangalore Dr SM Prasad , President of PEAK Dr Shaila Bhattacharyya, Vice President IAP Bangalore Dr Sumitha Nayak, Hon. Secretary IAP BPS Dr Priya Shivalli were felicitated. Certificates and mementos were given away to the Faculty. After a short tea break, Dr Vani took the next session on precocious puberty , followed by congenital hypothyroidism by Dr Suman Rath and final session was on Obesity by Dr Mounica Reddy. There was a Question and Answer Session for delegates, followed by lunch and that was the end of Programme.

Activities by PEAK Members

The CME programs under the flagship of PEAK

World Diabetes Day(WDD) celebration at Indira Gandhi Institute of Child Health, Bengaluru – 26 Nov 2022 - Dr Raghupathy P, Dr Vani H.N.

WDD is celebrated on 14th November every year. As a part of it, we conducted a comprehensive educational program at IGICH on 26 November, which had overwhelming participation from the children and their parents. Almost 120 children with diabetes, accompanied by their parents, attended the event, which was organized by Prof. P. Raghupathy and his team of doctors, including Dr Vani HN and endocrine Fellows. The program was inaugurated by Dr Sanjay KS, Director of IGICH, and started with a walkathon in the morning, followed by scientific talks given by eminent speakers. The topics discussed were 'Eating right for a better tomorrow' by nutritionist Ms Deepthi (dietician at KIER) and 'Psychological support for Type1 diabetes' by child psychiatrist Dr Eesha Sharma (Asst Prof. NIMHANS). Dr Raghupathy and Mr Dinakaran (Retired Senior Manager, Novo Nordisk) were felicitated.

The parents and children were educated about the usage of insulin pens, their advantages and ways to overcome the pitfalls. Parents had the opportunity to clear their doubts with regard to daily management of diabetes. Entertainment programs like a puppet show and dance events were thoroughly enjoyed by everyone. To make the occasion more memorable and lively, a drawing/ painting competition was held and prizes given.

These sweet kids also showcased their talents by dancing, singing, and performing yog asanas. Prizes were distributed to children who had achieved good HbA1c control, or excelled in academics and sports. At the end of the event, all the children were provided with free monthly insulin, lancets, glucometers and gifts. Overall, it was a memorable day for children, parents and our endocrine team.



Activities by PEAK Members

The CME programs under the flagship of PEAK

WDD program - Karnataka Institute of Endocrinology and Research, Bengaluru - 12/11/2022.

A program was organized on 12th Nov, with this year's WDD theme: "Education to protect tomorrow", by Dr Santhosh Olety, and dietitians Sharanya S Shetty, Shilpa C Parihar, Deepthi S, and Shruthi R. Almost 80 kids with T1D delightedly took part, along with their family members. The program started with an invocation song by one of our T1D kids, followed by an exhilarating magic show conducted by a parent, and many fun games, uplifting team spirit and delivering messages on how sharing knowledge and awareness can create a platform for a better tomorrow. Rotary Clubs announced that 45 more kids will be adopted and supported with diabetes supplies like analog insulin, pen needles, glucose testing strips and glucometers. Rotarians were introduced to T1D heroes - Dr Shuchy Chugh, Mr Anirudh S, Mr Nithin Somasundar, Mr Angad Chandhok, Mr Sahil Om Madan, Ms Geethanjali Rangaswamy and Ms Marielle Bostrom, conveying a strong message that uplifting people living with T1D with proper diabetes education and help, can enable them to achieve their dreams. The program ended with a talent show, gifts, and a healthy lunch.

Activities by PEAK Members

The CME programs under the flagship of PEAK

Patient Education program on Insulin pumps at Karnataka institute of Endocrinology and research, Bengaluru

Date 7/1/2023

An interactive education activity was organised at our Institute with the support from Medtronic India. 15 families with T1D kids attended the event. It was a 2.5 hr program which included talk on Evolution of Insulin pumps from basic to the most advanced pumps by Dr Santhosh Olety, practical pump demonstrations especially the advanced 780 G pump by Mr Deepak Bhatija followed by feedback and experience sharing by parents and their kids of using 715, 722, 620G and 640 G. Two families sharing their experience of using 780 G was enriching and same time provided platform for networking, exchange knowledge and solutions for potential challenges among parents. Discussion also included best pump settings and golden rules to be followed for optimal glycaemic outcomes. Session on 780 G was concluded with a remark that it is a continuous learning process for machine, users, and clinicians and time will improvise all.

Activities by PEAK Members

The CME programs under the flagship of PEAK

WDD 2022 Celebration - Endocare for Kids, Rajkot - Dr Zalak Upadhyay

Dr Zalak was able to spread awareness through Radio on 14 Nov, by giving an important message on diabetes in children and it's management. Juvenile Diabetes Foundation, Rajkot celebrated WDD on 13 Nov 2022, Sunday, with almost 400 kids. All the important topics were covered by endocrinologists in this camp. Dr Zalak gave a talk on "Importance of blood glucose monitoring, HbA1c and screening of complications". Dr Zalak's clinic, Endocare for Kids, celebrated WDD on 4th December 2022, Sunday at Rajkot. We invited all our T1D kids and their parents. We had 4 different tables for education on – Importance of glucose checking and CGM, Dietary management and carbohydrate counting, Insulin administration techniques and Insulin pump. Education was followed by tattoo making and interesting craft activity for kids, with special performances by our little stars, and lunch for all. The function was attended by almost 50 kids and their families.

Activities by PEAK Members

The CME programs under the flagship of PEAK

Sweet Little Stars Celebration

Apollo Children's Hospital, Chennai - Dr V Soundaram

As part of WDD celebration 2022, we organized an event in the Auditorium of our hospital. There were 3 academic sessions – 'Trouble-shooting high sugars', 'Mental health challenges in T1D', and 'Common mistakes in diet'. Miss Athira, a young playback singer, did mash-up for 15 mins. We had also organized games for the kids. The program was sponsored by Novo Insulin and Pulse Nutrition.

The Second Pediatric Pituitary Conference

Dr V Soundaram, Apollo Proton Cancer Center, Chennai.

Pituitary disorders are relatively rare in the pediatric age group, but need multi-disciplinary care. This meeting was organized to enhance the knowledge of pediatric endocrinologists, neurosurgeons and radiation oncologists handling such patients. It was conducted under the aegis of the Apollo Proton Cancer Center and ISPAE. Top experts from Indian and UK gave lectures to the approximately 70 doctors. There were no sponsors.

Activities by PEAK Members

The CME programs under the flagship of PEAK

WDD celebration at St. Johns Hospital, Department of Paediatric Endocrinology under the able guidance of Dr Poornima

World Diabetes Day was celebrated on 19 th November 2022 by the Department of Pediatrics in association with the Department of Medico Social Work. 25 children diagnosed with diabetes and their parents attended, and the programme was graced by our Associate Director of Hospital –Rev. Dr. John Thekkekara, Chief of Medical Services – Dr. Aravind Kasthuri, Chief of Nursing Services – Sr. Ria Emmanuel, HOD of Paediatrics – Dr. Chitra Dinakar, HOD of Paediatric Surgery – Dr. Subha A.M. and all the other team members of Pediatrics, Medico Social Work, and allied departments. The programme began with an invocation song,welcome address and inauguration by children and dignitaries. There were activities like dance and games as part of recreation and entertainment for children and their parents. The highlight of the day was Children's Talent Show where our Juvenile Diabetes children showcased their talents in the form of Yoga, Dance and Singing with great enthusiasm. Dr. Poornima, Asst. Professor, Pediatric Endocrinologist spoke regarding the importance of follow-up, treatment and diabetes education followed by session by Dr. Chitra Dinakar by addressing emotional, psychological, and parental issues of teenagers. Ms. Jisha Sara Jose, Medico Social Worker, Pediatrics, educated parents on importance of support group and addressed their social issues. The team from Novo nordisk provided free insulin pens for children and training session on usage of pen was provided. The programme was supported by various organizations like Child Vikas Foundation and Make a Wish Foundation who distributed gifts based on children's wish.

Activities by PEAK Members

The CME programs under the flagship of PEAK

CME by Dr Tejasvi Sheshadri

CME Venue- East point college of medical sciences and research centre,Avalahalli, Bangalore

Dr Seshadri was given an opportunity to give a talk for a paediatric CME conducted by the department of Paediatrics at East Point college of medical sciences, Bangalore. The CME's theme was Paediatric Pearls. Her topic was on Paediatric Obesity. She addressed nurses, MBBS students, interns, Paediatricians and doctors from other departments about the evaluation, management and complications of obesity. She also spoke about the diet in obesity and how prevention is key and what steps can be taken to prevent paediatric obesity. The rarer causes of obesity (endocrine obesity/ genetic obesity syndromes) were also highlighted. The CME was an interactive session with case based discussion at the end for the students.

Activities by PEAK Members

The CME programs under the flagship of PEAK

Educational Program for Young Diabetics at Department of Paediatrics, KMC, Manipal by Dr. Koushik Urala (Assistant Professor, Paediatric Endocrinologist) and team, Department of Paediatrics, KMC, Manipal.

Indian Council of Medical Research (ICMR), Govt. of India funded Young Diabetes Registry (YDR) Phase III in association with Department of Pediatrics & Pediatrics Endocrinology Clinic, KMC, Manipal has successfully conducted a full-day Educational Program for Young Diabetics on January 7, 2023 at Department of Paediatrics, KMC, Manipal.

Seventeen young diabetics (2-25 years old) have participated with their caretakers. Fasting blood sugar (FBS) and glycated hemoglobin (HbA1c) testing, along with anthropometric and vital parameters were done at the beginning of the program. The program was inaugurated with the comments of Dr. Shivashankara KN, Professor of Medicine and In-charge of YDR III at KMC, Manipal, and Dr. Leslie Edward Lewis, Professor, and Head, of the Department of Paediatrics, KMC, Manipal, followed by an introduction to the program by Dr. Koushik Urala H, Assistant Professor, Paediatric Endocrinologist, Department of Paediatrics, KMC, Manipal. Dr. Ajit Singh, Research Officer for ICMR YDR II at the Department of Medicine, KMC, Manipal, has participated in and coordinated the program well with the organizing departments.

Dr. Sharath K Rao, Pro Vice-Chancellor - Health Sciences, Manipal Academy of Higher Education, Manipal, and Dr. Padmaraj Hegde, Dean, Kasturba Medical College, Manipal, have guided the program as chief guest and guest of honor, respectively. Dr. Avinash Shetty, Medical Superintendent, Kasturba Hospital, Manipal, and Dr. Anand Venugopal, Chief Operating Officer, Teaching Hospitals, MAHE, Manipal, have supported the program entirely and have been our guests at the program. The educational sessions for our young diabetics were conducted with the help of the Department of Yoga, Centre for Integrative Medicine & Research, MAHE, Department of Clinical Nutrition & Dietetics and Department of Physiotherapy, Manipal College of Health Professions (MCHP), MAHE and Department of Ophthalmology, KMC, MAHE. This was followed by Yoga consultation & demonstration, diet demonstration for every meal with complete scientific nutritional knowledge, diabetic foot care awareness, and assessment and eye check-up for diabetic retinopathy by the experts at their respective stalls.

Self-introduction by young diabetics, inspirational talks, participation in fun games, quizzes, and cultural programs helped us to motivate the young patients and families to cheer up. Cultural programs by resident doctors of Paediatrics department added color to program. The winners of the events and games received the prize during valedictory by our guest of honor.

Food (breakfast, mid-snack tea, lunch, and high tea) , blood testing, educational sessions, insulin for one month were offered free of cost to all participants.

The patient speaks an interesting case report

Infantile hypophosphatasia : An exceptional disorder of bone mineralisation

Dr. Trishya Reddy, Fellow in Paediatric Endocrinology

Dr. Shaila Bhattacharyya, Consultant Paediatric Endocrinologist

Manipal Hospitals, Bengaluru

BACKGROUND:

Hypophosphatasia (HPP) is an extremely rare heritable genetic disorder that occurs due to a loss of function mutation of the ALPL gene located on chromosome 1 (1p36.1) that encodes for tissue non-specific alkaline phosphatase (TNSALP). Mode of inheritance can be either autosomal dominant or recessive. HPP can be classified into 6 forms based on the age of presentation, inversely proportional to the severity of the disease as perinatal, infantile, childhood (mild and severe), adult and odontohypophosphatasia.

CASE PRESENTATION:

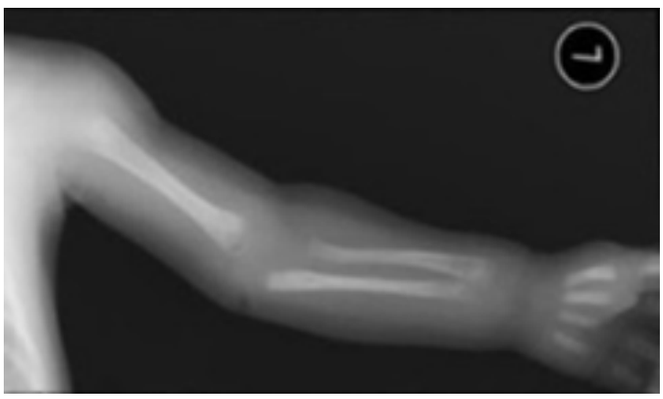
A 4 month old female infant, first born to a non-consanguineous marriage, presented with failure to gain weight since birth. Baby was delivered by an elective caesarean section in view of intrauterine fibroid with a birth weight of 3.06 kgs and cried immediately at birth. Baby developed physiological jaundice requiring phototherapy for 2 days. After administration of the birth vaccines, baby was discharged on daily oral supplementation of 400 IU of vitamin D.

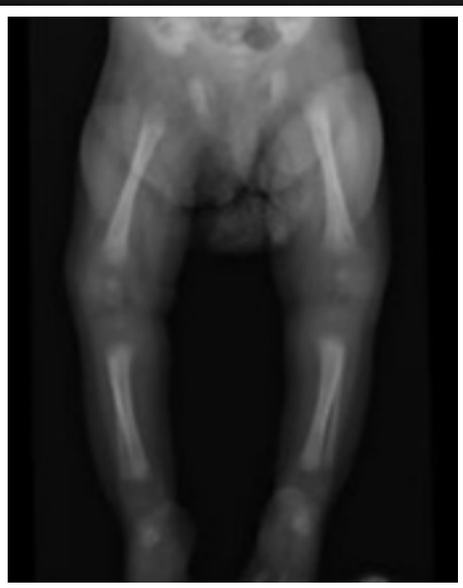
Baby did not regain her birth weight by day 10 of life and in fact had a weight loss of 0.66 kgs (22%) from the birth weight. Baseline investigations were carried out at 1.5 months of age in view of the weight loss despite adequate feeding and baby was found to have Urinary tract infection for which she was treated appropriately. Upon recovery, Micturating cystourethrogram was performed.

At 4 months of age, in view of persistent weight loss, investigations revealed serum calcium : 12.3 mg/dL, serum phosphorous : 6 mg/dL, PTH : 1.2 pg/mL, ALP : 10.7 IU/L and vitamin D : 51.29 ng/mL. Infant was advised admission and was treated with IV fluids and diuretics. Genetic test was sent.

On further investigations, serum calcium : 16.1 mg/dL, urine calcium creatinine ratio : 1.1 and ultrasound abdomen showed bilateral nephrocalcinosis. She was administered 1 dose of Inj. Zoledronate 0.05 mg diluted in 50 ml of normal saline. Repeat investigations showed, serum calcium : 12.7 mg/dL and urine calcium creatinine ratio of 0.74. Skeletal X-rays were done and showed generalised poor bone mineralisation.

The patient speaks an interesting case report





Clinical exome sequencing revealed heterozygous mutation of the ALPL gene with 2 variants, c.1303G>C in exon 11 and c.1471G>A in exon 12 confirming the diagnosis of infantile hypophosphatasia. Genetic tests of her parents has been sent and is currently awaited

PARAMETER				
S. Calcium (mg/dL)	12.3	16.1	12.7	10.5
S. Phosphorous (mg/dL)	6			5.1
ALP (IU/L)			10.7	23
PTH (pg/mL)	1.2			
Urine calcium creatinine ratio		1.1	0.74	

IV FLUIDS & DIURETICS

INJ. ZOLEDRONATE 0.05 MG

ALPL GENE MUTATION CONFIRMED

TREATMENT PLAN:

The definitive treatment for infantile hypophosphatasia is enzyme replacement therapy (ERT) with Asfotase Alfa, recombinant TNSALP which was approved for paediatric use in 2015. Recommended dose is 6mg/kg/week (either 1mg/kg/day for 6 days a week or 2mg/kg/day for 3 days a week) which is administered subcutaneously.

Strensiq, manufactured by Alexion pharmaceuticals is available in the form of vials with varying strengths as 18mg (0.45mL) , 28 mg (0.7mL), 40mg (1mL) and 80 mg (0.8mL). As the drug is currently unavailable in India, efforts are being taken by the parents to gather funds and import the drug from UK.

DISCUSSION:

Infantile HPP, presenting within 6 months of age is caused by a deficiency of TNSALP results in the accumulation of TNSALP substrates such as inorganic pyrophosphate (Ppi). Elevated extracellular levels of PPi blocks hydroxyapatite crystal growth leading to defective bone mineralisation. Infantile HPP is characterised by failure to thrive, hypotonia, rickets, craniosynostosis and vitamin B6 dependent seizures.

The initial responses to ERT are significant weight gain and improvement in radiological changes within 6 weeks of treatment. Adverse effects of asfotase alfa include injection site reactions, hypersensitivity reactions, lipodystrophy, ectopic calcifications and hepatitis. The dose can be increased to a maximum of 3mg/kg/day for 3 days a week.

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The patient speaks an interesting case report

A RARE CASE OF ATHELIA-SEN SYNDROME

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Mazumdar Shaw Medical Centre- Narayana Health City, Bangalore, India

INTRODUCTION:

Athelia or hypothelia means absence or underdeveloped breast nipple and Amastia means absence of breast tissue. There are a few causes for athelia namely Poland syndrome, Ectodermal dysplasia, Yunis-Yaron syndrome, Progeria, Al-Awadi Rass Rothschild syndrome and SEN syndrome.

We present a case of a 12.5year-old girl presenting with hypothelia and athelia with dysmorphic facial features, who on genetic test, was diagnosed to have SEN (Skin-Ear-Nipple) syndrome.

CASE REPORT:

A 12.5year-old girl born to non-consanguineous parents presented with abnormal development of the breast. There was no positive medical history in the past or in the family. The child attained menarche at 12 years. On examination: height:156cm (75th- 90thc), weight:40kilos (50thc), BMI:16.52kg/m^2, head to toe examination showed hypopigmented sparse scalp hair, pseudohypertelorism (growth in the medial canthus of the left eye), telecanthus (increased distance between the medial canthi), narrow palpebral fissure with flat nasal bridge, small and folded-over ears with normal hearing, widely spaced teeth, brachydactyly (short fingers), syndactyly (fusion of skin between the fingers) with dystrophy of the nails (brittle nails) and dry skin. Tanner stage: P2A1M1, Left side athelia and right side hypothelia with bilateral amastia. Vitals and systemic examination were otherwise normal for age. Investigations: bone age: 13.6years, hormonal evaluation were all within the normal limits ruling out hypogonadotropic hypogonadism: LH-5.8mIU/ml, FSH-8.3mIU/ml, 17OHP-1.6ng/ml, prolactin-14ng/ml, TSH-2.84 IU/ml, T4-10.5 g/dl, FT4-2.1ng/dl, ultrasound abdomen and pelvis showed normal kidneys, pubertal sized uterus and ovaries with endometrial thickness 4mm, plain CT scan skull showed lipoma over the roof of the nose. In view of the above clinical features, genetic testing (NGS) was sent, which detected a KCTD1 gene mutation which is consistent with SEN syndrome.

DISCUSSION:

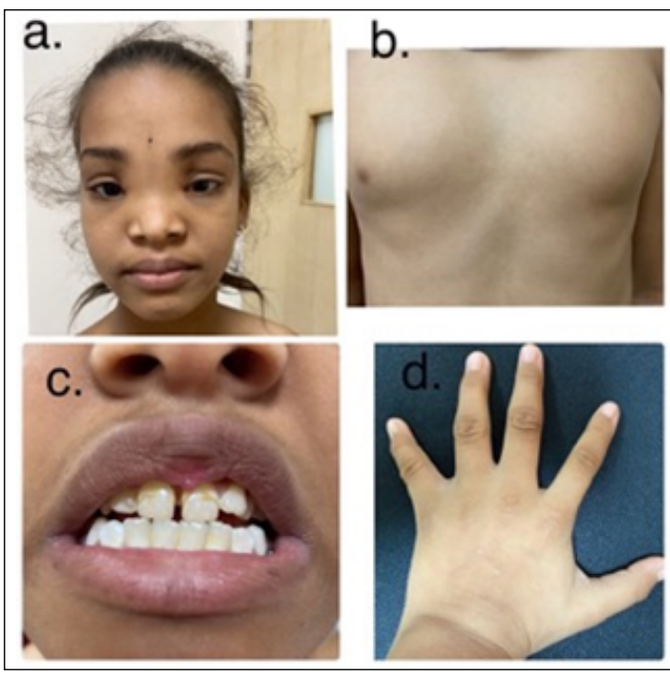
SEN (Scalp-Ear-Nipple) syndrome is a rare, autosomal dominant disorder characterized by a spectrum of congenital anomalies involving mainly the scalp, ear and nipple with less frequently involving other parts of the body. It was first described in 1978 by Finlay and Mark and is eponymously referred as Finlay Mark syndrome, hereditary syndrome of lumpy scalp, odd ears and rudimentary nipple syndrome.[1] It is caused by the mutation in KCTD1 gene, involved in the development of the ectoderm and thus the abnormalities of the ectodermal tissue.[2] KCTD1 gene (potassium channel tetramerization domain containing-1), inhibits the transactivation of the transcription factor AP-2 (TFAP2) and mutation in this TFAP2 causes cutis aplasia. The scalp lesions include aplasia cutis congenita which involves patchy abnormal areas on the scalp which are firm, raised, hairless nodules resembling a wound or ulcers but heal during childhood. The ear abnormalities include small ears, folded over, cup shaped with normal hearing along with underdeveloped or absent

The patient speaks an interesting case report

RESULTS

LIKELY PATHOGENIC VARIANT CAUSATIVE OF THE REPORTED PHENOTYPE WAS DETECTED

Gene (Transcript) *	Location	Variant	Zygosity	Disease (OMIM)	Inheritance	Classification
KCTD1 **(-)** (ENST00000408011.7)	Exon 2	c.97C>T **(p.His33Tyr)**	Heterozygous	Scalp-ear-nipple syndrome	Autosomal dominant	Likely Pathogenic



a. Pseudohypertelorism,telecanthus
b. Left Athelia with amastia,
right hypothelia with amastia
c. Widely spaced teeth with pigmentation
d. Brachydactyly, syndactyly

nipples (hypothelia/ athelia) or absent underlying breast tissue (amastia). Other features include telecanthus, narrow palpebral fissures, broad flattened nasal bridge, anteverted nares (nostrils that open to the front rather than downward), widely spaced or missing teeth, syndactyly, nail dystrophy, hypoplastic kidneys.[1,3]

The phenotypic features of SEN syndrome overlap most notably with MIM (Ulnar Mammary syndrome) and Ectrodactyly with ectodermal dysplasia and cleft lip/palate syndrome.

Our patient will require breast reconstructive surgery as the hormonal levels were normal and HRT (hormone replacement therapy) will be questionable.

CONCLUSION:

It is concluded that SEN syndrome is a rare genetic condition with genetic heterogeneity and to date, fewer than 15 independent cases are reported.

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The patient speaks an interesting case report

PAIN ABDOMEN: A COMMON SYMPTOM BUT AN UNCOMMON DIAGNOSIS!

Dr. Meghana N, Dr. Vani HN, Dr. Raghupathy P

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CASE REPORT:

Miss. J, an 8 year 5 month old Girl, presented to the Emergency Department with complaints of excess facial and body hair growth since past 3 months and complaints of pain abdomen of 1 week duration.Her parents had noticed excessive facial and body hair growth, predominantly over the upper lip, chin, upper back, hands and legs and in axilla and pubic region in the previous 3 months but doctor's consultation was not sought. Pain abdomen was severe, localized to the left flank, was associated with vomiting and had increased in severity since 1 week. She had no complaints of weight or skin changes. There was no history of drug intake, use of any ayurvedic medications or topical cream application.

On examination, she had tachycardia associated with pallor, and a blood pressure of 90/60mmHg. She had signs of virilization in the form of hirsutism with terminal hair over moustache area and chin, upper back (a modified Ferriman Gallaway score of 09), axillary hair growth and pubic hair (Tanner stage 3 . She had no acne, clitoromegaly, evidence of cushingoid features or neurocutaneous markers. Her height was 127.2 cm (25th to 50th centile, z score of -1.42) and weight was 20 kg (at 10th centile, z score of 0.017). Her Bone age was 12 years (TW-2). On per abdomen examination, diffuse tenderness and rigidity was present with no evidence of mass per abdomen.

Ultrasound abdomen revealed a complex heterogeneous mass on left renal region with surrounding haemorrhage. Following which a contrast enhanced computed tomography (CECT) of the abdomen was done, which showed a 9 x 8.5 x 10.5 cm heterogeneously enhancing left suprarenal mass with internal hemorrhages, with mass effect on the left kidney. Perinephric and retroperitoneal hematoma with moderate hemoperitoneum was also seen (figure 1). The right adrenal gland and kidney were normal and there were no focal lesions in the liver. CT chest and brain showed no evidence of metastasis.

Laboratory investigations revealed normal hematological and biochemical parameters. Morning (8 am) serum cortisol was 48.3 µg / dL (3-21 mcg/dl), serum dehyrdro-epiandrosterone sulfate (DHEAS) was 174 µg / dL (13-115 mcg/dL), serum total testosterone was 29.26 ng/dL (< 3-10 ng/dL), and serum adrenocorticotropic hormone ACTH was 105 pg/mL (10-60 pg/mL).

Laparotomy and left Adrenalectomy was done under stress dose coverage of hydrocortisone during perioperative period. Intra-op findings revealed clotted blood with large left adrenal tumor with left kidney found floating within the

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clotted blood. Tumor deposits were also found on the diaphragm, and resected completely. Gross examination showed grey brown soft tissue bits varying in size from 10 x 9.5 x 2.5 cm to 0.3 x 0.3 cm with hemorrhagic areas over the external surface was present (figure 2). On Microscopy, Diffuse sheets of large polygonal cells with large round nuclei were seen (figure 3). Also large areas of necrosis and haemorrhage with inflammatory infiltrate in the extra-adrenal adipose tissue was present (figure 4) accounting for a Weiss score of 4 suggestive of malignancy. Reticulin stain showed altered network in the tumor. Immunohistochemistry was positive for Inhibin, Melan A, Calretinin and Synaptophysin and and negative for Cytokeratin and Chromogranin A, confirming the adrenocortical origin. Ki-67 proliferative index was 7 to 8% in hot spots suggestive of malignancy.

According to ENSAT (European network for staging of adrenal tumors) staging she was diagnosed as a case of stage 3 adrenocortical carcinoma.

Following tumor resection her biochemical parameters normalized, Morning (0800 hours) serum cortisol was 15.5 µg / dL (3-21 mcg/dl), serum dehydroepiandrosterone sulfate (DHEAS) was 15 µg / dL (13-115 mcg/dL), serum total testosterone was 25.27 ng/dL (< 3-10 ng/dL), and serum adrenocorticotropic hormone ACTH was 34.3 pg/mL (10-60 pg/mL). She received 6 cycles of chemotherapy with Cisplatin, Etoposide and Adriamycin, along with radiotherapy to the abdomen – 45Gy over 30 fractions. FDG PET scan done after 1 month of completion of chemotherapy and radiotherapy showed no evidence of local recurrence or distant metastasis. She is on regular follow up since then and is currently disease free, 3 years after completing her treatment.

DISCUSSION:

Adrenocortical Carcinoma (ACC) is a rare but aggressive tumor. Its reported incidence being 0.2 - 0.3 new cases per 1 million children per year.[1,2] ACTs have a bimodal age distribution, with the first peak in the first decade and the second peak in the fifth decade of life.[3] Most cases are sporadic while about 50% of childhood adrenocortical carcinomas can be familial. Genetic predisposition syndromes that show an increased incidence of pediatric ACC include the Li–Fraumeni syndrome, Beckwith Wiedemann syndrome, multiple endocrine neoplasia type 1 or Carney complex.[4]

The Adrenocortical tumors have varied presentation either virilizing forms or presentation with Cushing's syndrome, or both. Most childhood ACC present with virilization (84.2%), with purely virilizing in 55%. This might be associated with overproduction of other adrenocortical hormones.[5]

Our patient presented with pain abdomen due to local tumor growth and signs of virilization associated with elevated serum DHEAS and serum cortisol levels. ACTH levels were also found to be mildly elevated in the present case, though non-ACTH-dependent hypercortisolism is the norm of adrenal malignancies, ectopic ACTH secretion by adrenal tumor cells can result in ACTH-dependent Cushing's syndrome and has been reported in few case reports.[6] Since she presented with acute pain abdomen, imaging studies were immediately done which established the cause, hence further biochemical investigations like dexamethasone suppression test were not performed.

Surgery is the cornerstone of the treatment in ACTs. Functional ACTs are presumed to cause suppression of the contralateral adrenal gland, and hence perioperative stress dose of intravenous Hydrocortisone is required.[7] Modified Weiss criteria is an established method for the diagnosis of ACC.[8] Out of nine histological criteria, three findings are required to make the diagnosis of ACC and our case fulfilled four Weiss criteria. The morphology was characteristic of ACC. No single immunohistochemistry marker is 100% sensitive or specific in diagnosis of ACC. Immunohistochemistry of the present case was positive for Inhibin, Melan A, Calretinin and Synaptophysin and negative for Cytokeratin and Chromogranin A, where calretinin positivity was 95% sensitive for adrenal cortex and chromogranin A is 100% sensitive for adrenal medulla, confirming the adrenocortiocal origin. Ki-67 proliferative index was 7 to 8% in hot spots, where Ki-67 index of >5% is suggestive of malignancy.

Although combination chemotherapy with etoposide and cisplatin was described in the postoperative management the role of chemotherapy is not yet

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established due to limited number of cases. Adjuvant therapy with mitotane (dichlorodiphenyldichloroethane) is an established option in advanced and metastatic ACC in adults, an insecticide derivative causing adrenocortical necrosis and tumor regression. However, its role in children pediatric ACC is not well established.[9]

Stage of the tumor strongly correlates with prognosis in ACC. Children presenting with stage I tumor have greater than 90% survival, and around 53% of those with stage II tumor are recurrence free at 5 years from diagnosis. Very few children present with stage III or IV disease but their prognosis is extremely poor. In general, younger patients who present early because of virilizing symptoms have a lower stage disease and, thus, demonstrate a better outcome.[5] Recently, Ki-67 proliferation index has been identified as the most important prognostic factor for recurrence-free survival.

ACC in children, due to the rapid development of symptoms they come to attention early, however, if not diagnosed and treated early, it can have a downhill course. Early diagnosis and aggressive management is utmost important in treating childhood adrenocortical carcinomas.

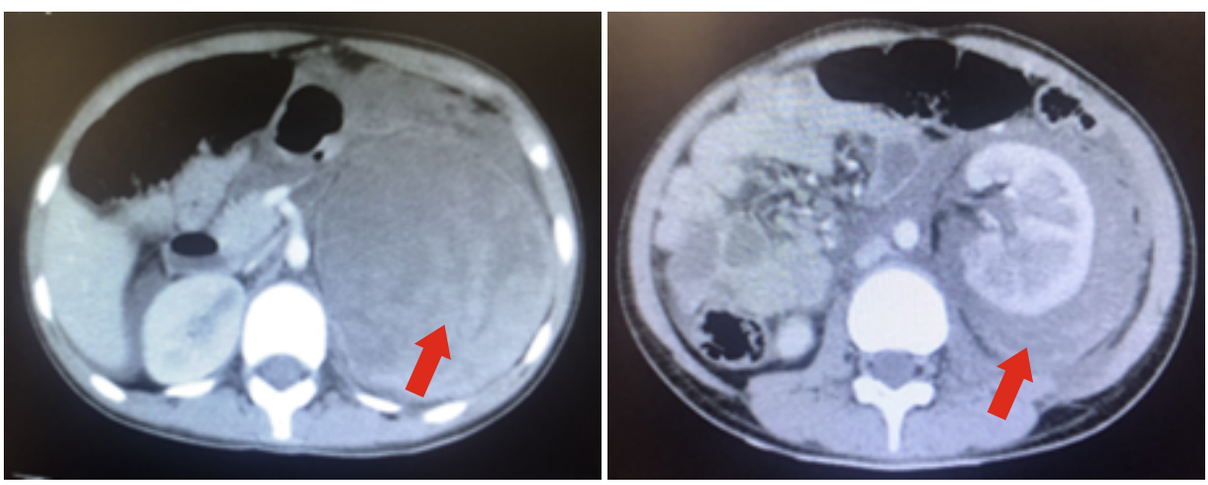

Figure 1: CECT abdomen showing a heterogeneously enhancing left suprarenal mass with internal hemorrhages, with mass effect on the left kidney. A Perinephric and retroperitoneal hematoma with moderate hemoperitoneum is also seen.

Figure 2: Gross appearance of the excised tumor weighing 500 grams with greyish brown soft tissue bits varying in size from 10 x 9.5 x 2.5 cm to 0.3 x 0.3 cm and hemorrhagic areas over the external surface.

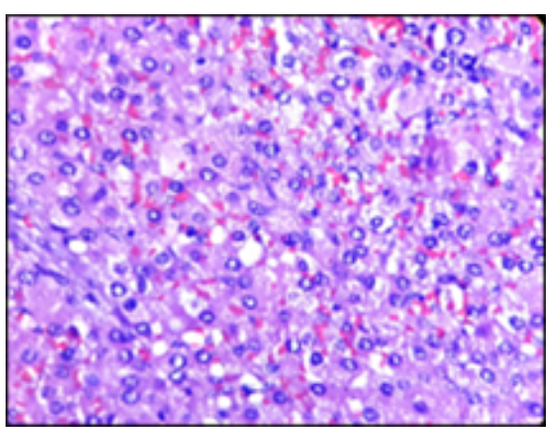

Figure 3: On microscopic examination of the resected tumor, diffuse sheets of large polygonal cells with large round nuclei, stippled chromatin and moderate eosinophilic cytoplasm was seen.

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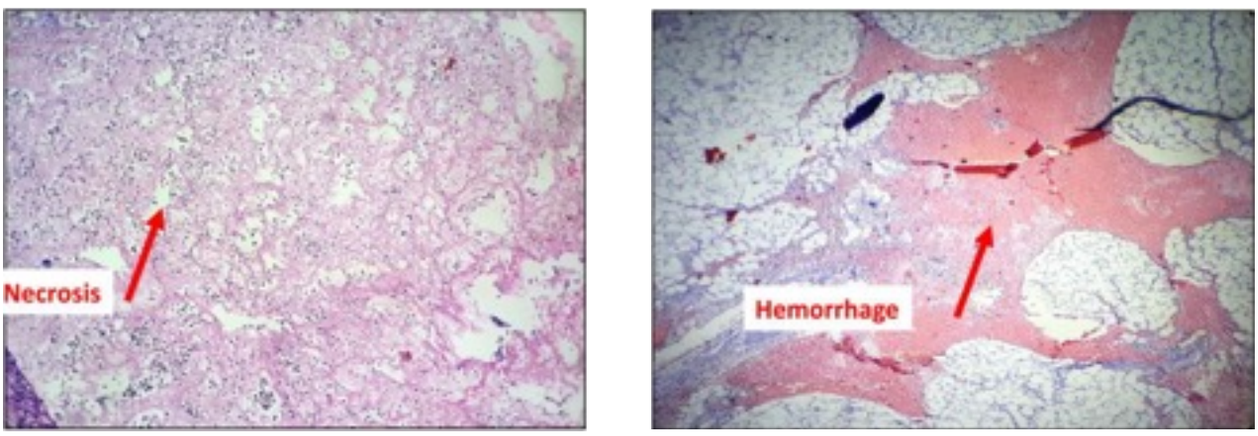

Figure 4: Microscopic examination of the resected tumor showing large areas of necrosis with focal areas of viable tumor cells and areas of haemorrhage with inflammatory infiltrate in the extra-adrenal adipose tissue.

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The patient speaks an interesting case report

Story of a drowning heart – an unusual manifestation of acquired hypothyroidism

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ABSTRACT:

Thyroid hormones play an important role in normal childhood growth and development. Slow linear growth and weight gain are the common presentation of juvenile acquired hypothyroidism (JH). Unusual manifestations such as precocious puberty, pericardial effusion, calf hypertrophy, enlarged pituitary are rare. Here we present a 17-year 8month old girl with acquired hypothyroidism who presented with massive pericardial effusion.

CASE DESCRIPTION:

A 17 year 8 month old female child presented with shortness of breath and generalized swelling of the body for 2 weeks, child was also found to have easy fatigability and decreased activity since 3 months. For these complaints she visited a cardiologist and was evaluated. Base line investigations showed anemia (microcytic hypochromic type), with normal ESR and albumin. A chest x-ray was performed which demonstrated a large globular heart (figure 2). An electrocardiogram (EKG) showed a ventricular rate of 50 beats/ min, normal PR/QRS/QTC intervals and low voltages in all leads. An echocardiogram obtained shortly after admission demonstrated a large pericardial effusion with cardiac tamponade and right ventricular diastolic collapse (RV size 1.1cm) with normal biventricular function (figure 3). Subsequently pericardiocentesis was done (approximately 500mL of serous fluid) following which symptoms of shortness of breath improved. Thyroid function test revealed TT4 < 0.9 mcg/dl (5.1 - 14.1 mcg/dl), TSH > 100 mIU/ml (0.7 - 6.4 mIU/ml), there by started on thyroxine at 72 mcg/m²/day. Repeat ECHO post pericardiocentesis showed no effusion, following which child was referred to our institute for endocrinology consultation.

On arrival to our hospital, she was hemodynamically stable, physical examination revealed coarse facies, (fig 1) dry skin, hoarse voice, heart rate of 62 beats/min and a blood pressure of 110/60 mmHg . Her height was 147 cm (Z score -1.77) and her weight was 47 kg (Z score -0.45) and BMI is 21.75 (Z score 0.31). Her bone age was 14 years and her reflexes had a markedly delayed relaxation. The thyroid stimulating hormone (TSH) was elevated 100 mIU/ml (0.7 - 6.4 mIU/ml) with a free thyroxine of 0.43 ng/dl (0.8 - 2.0 ng/dl). In addition, the child had high titers of anti thyroperoxidase antibodies 398 IU/ml (upto 34 IU/ml) indicating autoimmune hypothyroidism. Usg thyroid showed altered parenchymal echoes with increased vascularity suggestive of thyroiditis. Hence child was continued on thyroxine 72 mcg/m²/day (100 mcg OD). On followup at 4 weeks thyroid stimulating hormone (TSH) was 5.13 mIU/ml (0.7 - 6.4 mIU/ml) with free thyroxine of 1.43 ng/dl (0.8 - 2.0 ng/dl) and total thyroxine of 10.45 mcg/dl (5.1 - 14.1 mcg/dl). Hence child is continued on same dose of thyroxine (72 mcg/m²/day) and is advised to be on routine follow up with cardiac and endocrine team.

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DISCUSSION:

Hypothyroidism presents with a myriad of subtle and nonspecific manifestations like weight gain, poor concentration, depression, fatigue, muscular weakness, menstrual irregularities and short stature. There are some unusual manifestations of hypothyroidism including Kocher-Debre-Semelaigne syndrome, multicystic ovaries, massive pericardial effusion, hypothyroid ophthalmopathy, Van Wyk-Grumbach syndrome, hashimoto's encephalopathy and pseudotumor cerebri.

Although mild pericardial effusion is a common cardiovascular manifestation of hypothyroidism, massive pericardial effusion is an uncommon occurrence[1] with the majority of cases occurring during the neonatal period or in children with Down syndrome[2,3]. Aside from neonates and children with Down syndrome, case studies show that 50-73% of paediatric patients with hypothyroidism have pericardial effusions. Pericardial effusion (PE) in hypothyroidism is a type of polyseropathy characterised by albumin extravasation and insufficient lymphatic drainage. Effusions occur as a result of increased albumin capillary leakage in hypothyroid patients, which can result in a slow buildup of protein-rich fluid in the pericardial space[4]. Though it has been reported in both adults and children, cardiac tamponade in hypothyroid patients is extremely rare, most likely due to the slow accumulation of fluid and the pericardium's marked distensibility[5,6]. Triiodothyronine binds to its nuclear receptor, the thyroid hormone receptor, and promotes the expression of several gene products in the heart, including alpha myosin heavy chain, beta-1 adrenergic receptor, voltage gated potassium channels, and a sarcoplasmic reticulum calcium ATPase[7]. Changes in the expression of these proteins are responsible for the commonly observed cardiac signs and symptoms of either thyroid hormone excess or deficiency. The standard treatment for effusions with hemodynamic compromise was pericardiocentesis. Treatment of hypothyroidism is with oral L-thyroxine replacement which resolves the effusion within 2-12 months[8].

CONCLUSION:

Paediatricians should be aware of the symptoms and signs of hypothyroidism. Screening of children with suspected hypothyroidism with simple thyroid function tests will help in early diagnosis and prevent the child going through complications arising due to long standing untreated hypothyroidism.

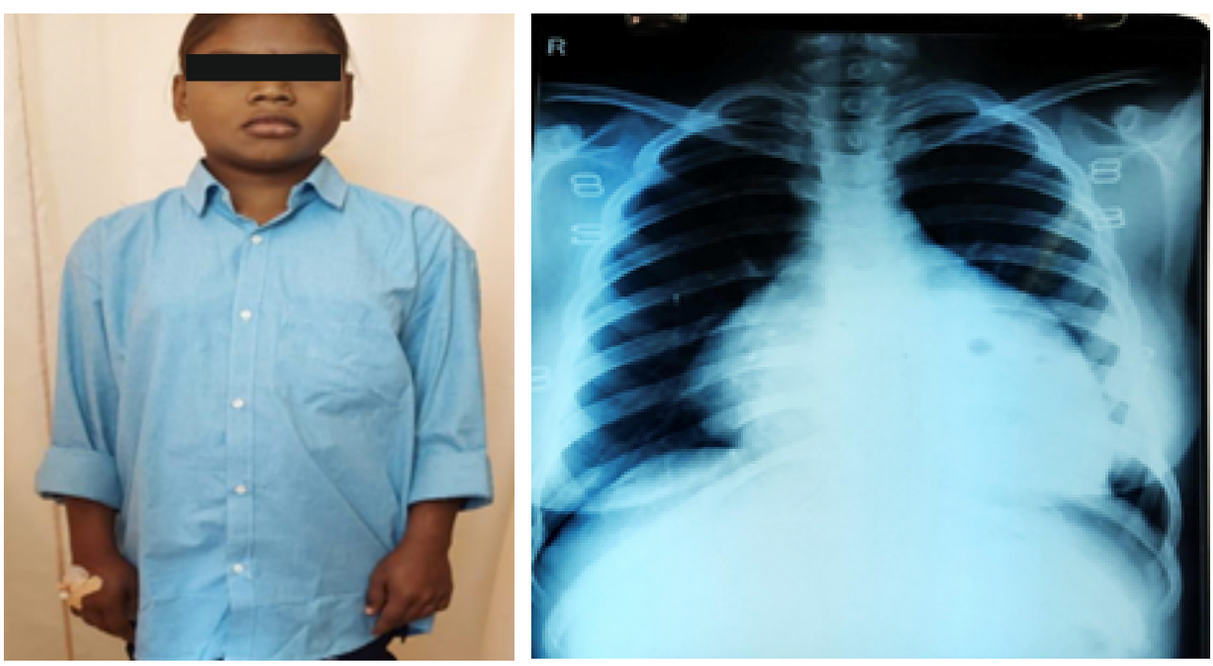

Figure 2: Chest X ray showing massive pericardial effusion

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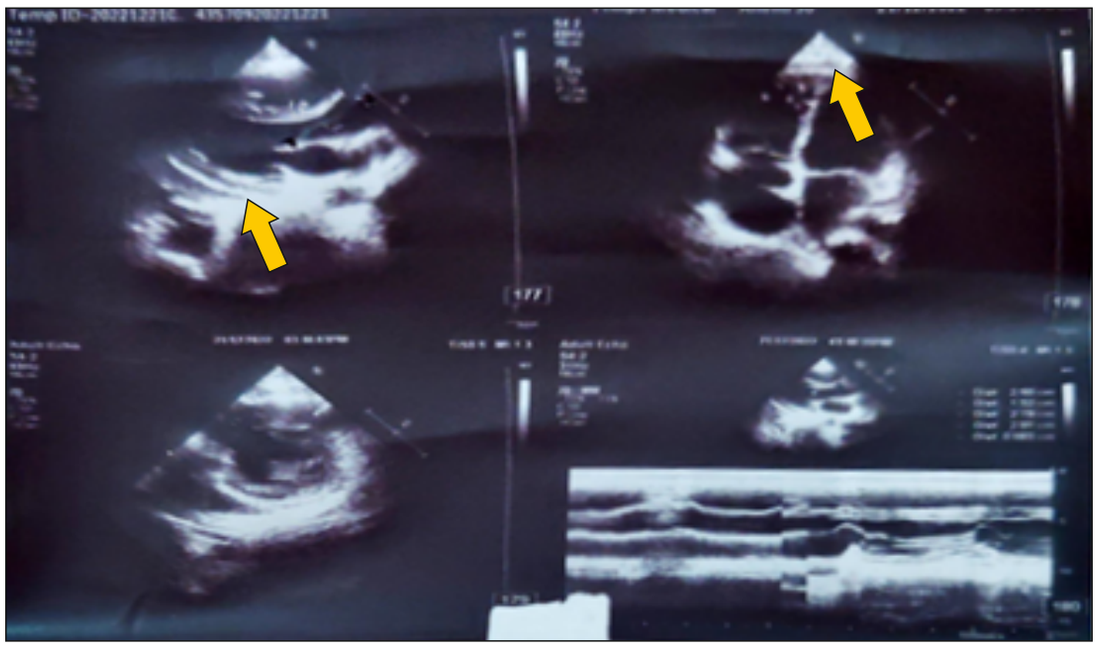

Figure 3: Echo showing pericardial effusion- (yellow arrows)

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The drug speaks

ZOLEDRONIC ACID - AN EFFICIENT BISPHOSPHONATE

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INTRODUCTION:

Bisphosphonates (BPs) have been widely utilised since the 1990s, and regarded as a cornerstone in the treatment of osteoporosis [1]. Other than osteoporosis in adults, this class of medication has also been used to treat Paget's disease of the bone, multiple myeloma, hypercalcemia, and bone metastases [2] BPs have been used more frequently in children with primary and secondary osteoporosis as well as other skeletal abnormalities since the osteogenesis imperfecta (OI).

In children with osteoporosis, zoledronic acid (ZA), a more potent third generation BP, can be used safely and effectively. When compared to Pamidronate, Zoledronic acid treatment is easier and more convenient to use because it is administered as a single intravenous infusion over a shorter duration of 30 minutes, with a longer interval between infusions, this makes Zoledronic acid an efficient treatment option. This article discusses Zoledronic acid's pharmacological properties, indications, dosage recommendations, and side effects.

MECHANISM OF ACTION:

Zoledronic acid is a nitrogen-containing Bisphosphonate of the third generation; structurally, all BPs require a phosphorus-carbon-phosphorus core and various side chains, with a hydroxyl group at the R1 position (Figure 1A). The potency of anti-resorption and the avidity with which the BPs attach to bone are determined by the substitution of side chains at R1 and R2. Because Zoledronic Acid has a cyclic side chain, a heterocyclic imidazole group attached to the R2 position (Figure 1B), it is more potent than other BPs. ZA, like other nitrogen-containing BPs, inhibits farnesyl pyrophosphate synthase (FPPS), a key regulatory enzyme required for osteoclastic formation and function, inhibiting bone resorption and inducing osteoclast apoptosis.

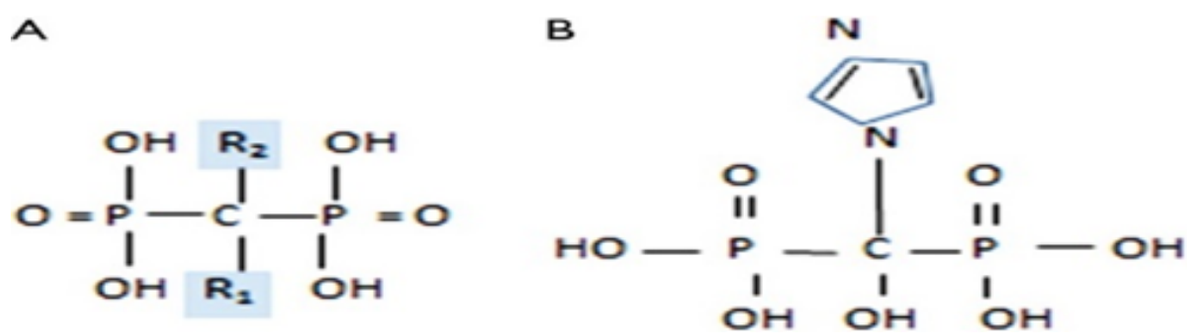

Figure 1: Chemical structures of BP and ZA. (A) General structure of BP. (B) structure of ZA with an imidazole-ring side. BP, bisphosphonate; ZA, zoledronic acid

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PHARMACOKINETICS[3]:

1. After intravenous infusion, plasma concentrations of ZA increase rapidly and rapidly decline to <1% of maximal concentration after 24 hours.
2. ZA is not metabolized and does not inhibit CYP enzymes.
3. About 55% of the dose is taken up by bone where it is retained for years and released back into the systemic circulation very slowly.
4. The remaining 45% of a dose is excreted unchanged in urine within 24 hours.
5. As renal excretion is the main route of elimination, ZA dose should be reduced and used with caution when creatinine clearance is <60 mL/min.
6. ZA is contraindicated in patients with creatinine clearance <35 mL/min or evidence of acute renal impairment.

INDICATIONS

Osteoporosis Primary · Osteogenesis imperfecta · Fibrous dysplasia **Secondary** · Glucocorticoid induced osteoporosis · Immobility induced osteoporosis · Cerebral palsy
Spinal cord injury
Duchene Muscular Dystrophy
Hypercalcemia due to · Vitamin D toxicity · Malignancy induced hypercalcemia

Table:1 Indication for Zoledronic acid use in paediatric age group [4].

DOSAGE

I. For primary osteoporosis

0.1 mg/kg/year divided into 2 doses per year given as 0.05 mg/kg/dose every 6 months [5].A lower starting dose of 0.025mg/kg given 3 months apart followed by 0.05mg/kg 6 months later can be followed.

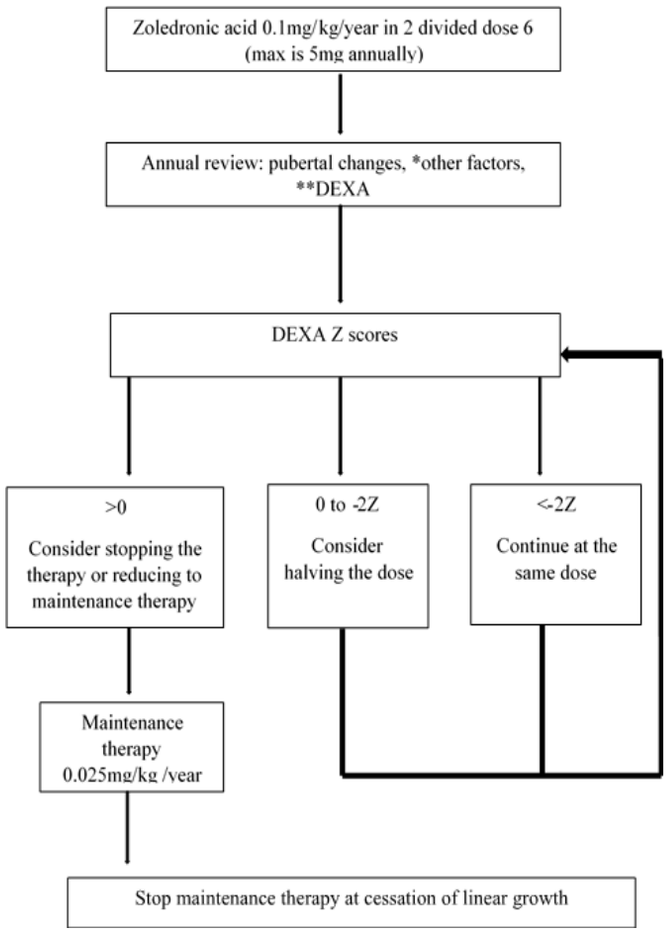

Figure 2: Flow chart for use of zoledronic acid in primary osteroporis [5] Note:*Other factors Fracture rate, bone pain, mobility; **DEXA- Dual-energy X-ray absorptiometry

SIDE EFFECTS:

1. Acute phase reaction (APR) - which manifests as flu-like symptoms such as low grade fever, nausea, myalgia and bone pain, or fatigue, is the most common adverse effect of BP and usually occurs within 48 hours of the first infusion.
2. Hypocalcemia and hypophosphatemia- A low vitamin D level appears to be a strong risk factor for APR, pain after BP infusion, and hypocalcemia. As a result, having sufficient vitamin D level greater than 30 ng/dL prior to BP treatment is critical. Calcium supplementation should be given both before and after the infusion to reduce the risk of post-infusion hypocalcaemia.

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II.For secondary osteoporosis.

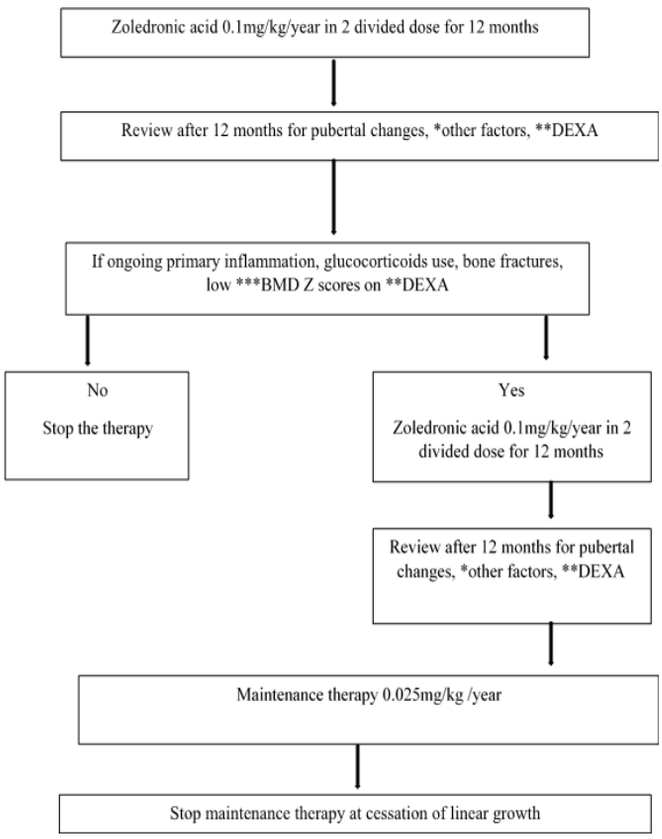

Figure 3: Flow chart for use of zoledronic acid in secondary osteroporis [5] Note; *Other factors Fracture rate, bone pain, mobility; **DEXA- Dual-energy X-ray absorptiometry; ***BMD done mineral density.

3. Atypical femoral fractures and osteonecrosis of jaw – Long-term bisphosphonate use has been linked to atypical sub trochanteric femoral fractures and jaw osteonecrosis in adults, but there have been very few reports of similar lesions in children.

4. Others- Oral/ esophageal ulcers, teratogenic effects, renal failure, atrial fibrillation more common in adults

MONITORING WHILE ON ZOLEDRONATE:

Yearly once

1. Dental
2. Ophthalmological evaluation
3. Hearing evaluation
4. X- ray- lateral spine and one of the limb to see for zebra lines
5. BMD (2yearly once) to look for improvement

SUMMARY:

Zoledronic Acid is a highly potent anti-resorptive bisphosphonate with superior efficacy in fracture reduction when compared to other bisphosphonates. Its application in children has progressed beyond primary and secondary osteoporosis. It should be used with caution, preferably with the advice of an expert, because there have been few long-term studies determining its safety and efficacy; therefore, more research is needed to determine the optimal dosing regimen and duration of therapy that will result in positive outcomes for children with these conditions.

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The drug speaks

TEPLIZUMAB - GAMECHANGER IN TYPE 1 DIABETES MELLITUS?

On November 17th 2022, FDA approved Teplizumab, the first drug that can delay the onset of stage 3 of type 1 diabetes(T1D) in adults and children aged 8 years and above who currently have stage 2 of T1D.

Stages of evolution of T1D are as follows:

Stage 1 - multiple islet auto-antibodies, normal blood glucose, no symptoms.

Stage 2 - abnormal glucose tolerance, usually no symptoms.

Stage 3 - blood glucose above ADA diagnostic thresholds.

Stage 4 - established T1D.

Efforts to delay progression from stage 1 or stage 2 to stage 3 diabetes come under secondary prevention. Several immunomodulatory agents are being studied for prevention of T1D. Teplizumab is a monoclonal antibody targeting T cell surface marker CD3, believed to stabilize beta-cell function and delay the progression of T1D to clinical disease.

Screening for pre-symptomatic T1D:

The feasibility of large scale population screening for risk of T1D is being evaluated in several countries. The aim of such programs would be to decrease morbidity and mortality rates due to DKA and prepare families for a planned transition to insulin therapy. An intermediate step toward population screening would be to routinely screen family members of those affected with T1D, keeping in mind that 85% of those with T1D do not have a positive family history.

Teplizumab Randomized Controlled Trial:

The TrialNet TN10 anti-CD3 prevention trial enrolled 76 relatives at risk for T1D. They belonged to an age range of 8 to 49 years and had 2 positive autoantibody tests within 6 months prior to enrollment. 29/44(61%) of the teplizumab group were <18 yrs old. Participants received either intravenous

infusions of teplizumab or saline for 14 consecutive days. Each infusion takes about 30 minutes and is followed by a 2 hour observation period. The participants were followed up over an extended period of time (median of 923

days) during which 25/32(78%) of the placebo-treated and 22/44(50%) of those treated with teplizumab developed T1D.

The drug speaks

Dosing

DAY 0	51 µg/m2
DAY 1	103 µg/m2
DAY 2	207 µg/m2
DAY 3	413 µg/m2
DAY 4-13	826 µg/m2
Total dose – 9mg/m2 For a person with 70kg body weight this comes to a total of approximately 18mg.	

Efficacy: Median age of participants who received the drug was 13.9 years. Extended follow up of trial participants showed a median time to diabetes of 5 years compared to 2 years in placebo treated participants with 50% of teplizumab treated participants not being diagnosed with T1D compared to 22% of those treated with placebo. 18% of teplizumab treated patients were followed up for more than 5 years and yet did not develop T1D compared to 6% of placebo-treated participants. Beneficial effects of teplizumab were noted as improved beta cell function, and increase in total and early insulin secretion rates and an overall better beta cell glucose sensitivity in those who progressed to clinical diabetes.

Adverse effects:Self-limiting lymphopenia and EBV-reactivation were noted in a number of participants treated with teplizumab.

Take home points: Teplizumab offers a glimmer of hope in the prevention of rapid progression to overt T1D in susceptible individual who maybe identified during mass population/family screening. Immunomodulation of beta cell function might delay the diagnosis of T1D by several years leading to decreased burden of diabetes on the families affected.

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Publications by Members

Dr Soundaram V presented "A case of thyrotropic pituitary adenoma unresponsive to Octreotide" along with neurosurgeon Dr.Roopesh Kumar and Dr.Vijayasarathi at The Pituitary Update Course 2022, at Estonia, Europe in October 2022.

Kubsad P.S, Hebbal Nagarajappa V, Soodhana Mohan D. A rare case of adolescent girl with beard- PCOS with a difference: “HAIR-AN Syndrome”. Dubai Diabetes Endocrinol J 2022;28:147-150.

Pachapure SS, Badiger S, Tadakanahalli S, Franco ED, Manthale A, Kulkarni V. Neonatal diabetes mellitus with congenital hypothyroidism (NDH) syndrome caused by GLIS3 mutation: A case report and review of literature. J Pediatr Endocrinol Diabetes 2022;2:86-9.

Upcoming Events

Information on upcoming Biennial meet in Bengaluru ISPAE 2023

Dear friends,

Greetings from the Organizing Committee of ISPAE 2023!!

It is indeed with great pleasure that we invite you to the 8th Biennial meeting of ISPAE to be held at Bengaluru, on 17 - 19th November 2023. Distinguished experts from international bodies, viz., European Society of Paediatric Endocrinology (ESPE), Asia Pacific Paediatric Endocrine Society (APPES), and International Society for Paediatric and Adolescent Diabetes (ISPAD) and reputed national speakers will be sharing their knowledge and expertise at this prestigious event. We do not need to remind you that this will also be the first physical conference after 4 years, hence we presume that you will be happy to attend this memorable event, and will grace it in large numbers.

The Paediatric Endocrinology for Trainees (PET) School will be organized as a residential 3 day Pre-Conference Academic Activity (14 - 16th November 2023), with Dr Ahila Ayyahoo as the Convener and Dr Shaila Bhattacharyya the Co-Convener. We shall be enrolling nearly 40 Clinical Fellows currently training in Paediatric Endocrinology in various centres in India and also the APPES region. Various topics related to growth, diabetes and other endocrine disorders will be covered during this training programme. This is being arranged amidst the green, sylvan surroundings of a natural resort close to Bangalore International Airport.

Details of both these meetings are available on our website www.ispae2023.com.

We extend a hearty welcome to you, one and all! Please do attend and enjoy the academic feast and our hospitality! We are looking forward to your visit!

With best wishes,

Yours sincerely,

Dr Shaila Bhattacharyya
Organising Chairperson

Dr Vani HN
Organising Secretary

SPEAK

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