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BACKGROUND: Fracture events in older adults are important opportunities for secondary prevention. In response to national (HEDIS) quality metrics in 2008, our medical group implemented a fracture prevention program, identifying women age ≥ 65 y who experienced a fracture and targeting them for osteoporosis screening or treatment within six months. In 2015, we added an outreach program for “high-risk secondary fracture prevention” targeting women age 60-85y and men age 70-85y for osteoporosis therapy within 6 months after a hip, pelvic, humerus, wrist or vertebral fracture. This study examines whether targeting “high-risk fracture” in women and men results in higher treatment rates following a non-vertebral major osteoporotic fracture.

METHODS: This retrospective study was conducted using data from women age 60-85y and men age 70-85y who experienced a fracture of the hip, humerus, and wrist in 2013-2014 (Cohort 1, the era of our HEDIS-only program) or 2015-2016 (Cohort 2, the era of our added “high-risk secondary fracture prevention” program). We excluded patients with primary bone disorders or metastatic cancer and those with osteoporosis treatment in the year prior to fracture. Osteoporosis drug therapy (oral/IV bisphosphonates, denosumab, raloxifene or teriparatide) initiated within six months after the fracture date was assessed. Differences between groups were compared using the chi-squared test, and multivariable logistic regression was used to examine predictors of treatment.

RESULTS: There were 5727 (Cohort 1) and 6469 (Cohort 2) adults identified with hip, humerus, or wrist fracture (high risk fracture). Wrist fracture was the most prevalent fracture in women and hip fracture the most prevalent in men. Osteoporosis treatment initiation within 6 months of the fracture date was achieved for 38% of women and 13% of men in Cohort 1 and 37% of women and 25% of men in Cohort 2. Among women age 60-64, treatment increased from 14% (Cohort 1) to 25% (Cohort 2). Overall, fracture in the later era (2015-2016) was associated with a slightly lower odds of post fracture treatment initiation (adjusted odds ratio OR 0.8, 95% confidence interval (CI) 0.7-0.9) in women 65-85y; however, a much higher odds of treatment was seen (OR 2.3, 95% CI 1.9-2.9) for men 70-85y. Older age, hip fracture, and past osteoporosis therapy were also associated with greater odds of treatment within 6 months.

CONCLUSION: Targeted high-risk fracture intervention resulted in a 2-fold increase in osteoporosis treatment after major non-vertebral osteoporotic fracture in men 70-85y and women 60-64y, the demographic subgroups not previously targeted by HEDIS-based intervention. However, treatment of fractures in women already targeted by HEDIS-based intervention did not increase. Future studies should address potential barriers to treatment and assess the impact of added high-risk fracture outreach on adherence to therapy.

Pediatric Endocrinology

PEDIATRIC PUBERTY, TRANSGENDER HEALTH, AND GENERAL ENDOCRINE

We Mind Your Step: Understanding and Preventing Drop-Out in the Transition from Paediatric to Adult Tertiary Endocrine Healthcare

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Introduction Transition from paediatric to adult endocrinology is a challenge for adolescents, their families and their healthcare professionals. Previous studies show that up to 25% of young adults with endocrine disorders are lost to follow-up once they move out of paediatric care. This poses a health risk for young adults, as lack of medical treatment and surveillance can have both psycho-social and physical consequences. Apart from absenteeism from school or work, this can lead to serious and expensive medical complications like Addison crisis.

Methods In 2019 we studied electronic medical records of 387 patients who were over 15 years old when they attended the paediatric endocrine outpatient clinic (OPC) of our medical centre in 2013-2014. We collected data from medical charts, the hospital digital agenda and medical correspondence.

Results Of 387 adolescents, 161 (42%) did not need adult endocrine follow-up because paediatric endocrine care was only puberty- or growth-related. Forty-six patients did not enter regular transition because they 1) participated in a pilot to improve transition (N=10), 2) had intellectual disability (ID) and transferred to ID care (N=28), or 3) died (N=8, mostly cancer-related). Hundred-and-eighty patients entered regular transition: 49 (27%) to a regional hospital and 131 (73%) within our university hospital.

Of these 131 patients, 33 (25%) were lost to follow up; in 24 of them (73%), the invitation for the adult OPC had never been sent. Loss to follow up occurred when three subsequent critical steps failed: 1) the adult endocrinologist had not received or read the paediatrician's referral letter and/or had not invited the patient; 2) the paediatrician had not checked whether the appointment was really made and received by the patient and 3) the patients and/or caregivers had not alarmed the hospital when no invitation for an appointment was received.

Conclusion We found a 25% dropout during transfer from paediatric to adult tertiary endocrine care. Starting the transition process early and in a structured manner, as well as assigning a transition coordinator, can prevent part of the dropouts. However, 73% of all dropouts appeared to be attributable to failure of practical, logistic steps. In order to prevent this part of the dropouts, we provide practical recommendations for all three parties involved:

1) the adult endocrinologist should carefully read paediatricians' letters and check whether action is required (i.e. check whether an appointment is requested)

2) the paediatrician should ascertain whether the appointment is really made and received by the patient

3) the patients and/or caregivers should be instructed to alarm the hospital when they do not receive the appointment.

These actions require relatively little effort and may prevent the part of drop-outs that is caused by logistic failures.

Pediatric Endocrinology

PEDIATRIC ENDOCRINE CASE REPORTS I

Twins with a Homozygous Variant of ARNT2, This Is a Known Saudi Mutation (KSM) of Webb-Dattani Syndrome

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Webb-Dattani syndrome (WEDAS) is an autosomal recessive disorder caused by mutation in the ARNT2 gene characterized by frontotemporal hypoplasia, globally delayed development, and pituitary and hypothalamic insufficiency. The condition is reported to be associated with consanguinity and with Saudi Arabian ancestry. We presented twin baby girls with developmental delay, seizures, and microcephaly. They have also hypopituitarism in the form of diabetes insipidus and hypocortisolism, also they have cortical blindness. Their brain MRI shows brain atrophic changes and delayed myelination thin corpus callosum, and small pituitary gland and absence posterior high signal spot and pituitary stalk. Genetic testing by Exome sequencing was done and it shows a homozygous variant of ARNT2 (ARNT2:NM_014862:exon3:c.147-1G>A). One of this twin her condition deteriorated with uncontrolled seizures and spasticity and died at age 22 months. Conclusion: we report another cases of the ARNT2 mutation in a Saudi family illustrating the disease of webb-dattani Syndrome with seizures and hypopituitarism and severe visual impairment and global developmental delay.

Tumor Biology

TUMOR BIOLOGY: GENERAL, TUMORIGENESIS, PROGRESSION, AND METASTASIS

The Secretory Vesicle Membrane Protein, CYB561, Promotes the Growth and Metastatic Potential of Castration-Resistant Neuroendocrine Prostate Cancer

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An increase in the population of neuroendocrine (NE) differentiated (NED) cells and their secretory products are closely correlated with prostate cancer (PCa) resistance to

existing therapies and eventual progression to castration-resistant PCa (CRPC). It is hypothesized that NED cells secrete neuropeptides that support tumor growth and induce aggressiveness of adjacent proliferating tumor cells through a paracrine mechanism. A gene that is constitutively expressed in secretory vesicles of NE cells, and has been previously found to be highly expressed in CRPC and cancer of several tissues is *Cytochrome b561 (CYB561)*. The *CYB561* gene encodes a secretory vesicle transmembrane protein that primarily functions in the regeneration of ascorbic acid, a necessary step in the α -amidation activation process in the biosynthesis of most neuropeptides. The *CYB561* protein also exhibits ferriredoxase activity and may contribute in regulating iron transport and metabolism, which are two other pathways often dysregulated in cancer. These findings led us to hypothesize that *CYB561* may be a key player in the NE differentiation process that drives the progression of prostate cancers into the more aggressive NE subtype. In our study, we found that *CYB561* expression is higher in metastatic and NE PCa (NEPC) models compared to normal prostate epithelia, and that its expression is not affected by androgen treatment or steroid deprivation. Lentiviral-mediated knockdown of *CYB561* in the NEPC cell line, PC-3, decreased the expression of genes involved in NE differentiation and labile iron pool storage, decreased cell proliferation, reduced cell survival in a colony formation assay, and slowed down cell migration in a wound-healing assay. Treatment of normal prostate epithelial cells, PNT1A, with conditioned media from *CYB561* knockdown PC-3 cells led to a decrease in proliferation rate when compared to treatment of PNT1A cells with media from *CYB561* expressing (control) PC-3 cells. Taken together, our findings demonstrate the role of *CYB561* in supporting the growth and metastatic potential of NEPC cells, and highlights the potential use of *CYB561* as a therapeutic target and biomarker that can be used to identify more aggressive disease.

Pediatric Endocrinology

PEDIATRIC ENDOCRINE CASE REPORTS II

A Case of Growth Hormone Deficiency in Sturge-Weber Syndrome

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Introduction: Sturge-Weber syndrome (SWS) is a congenital neurocutaneous disorder characterized by a port wine stain on the skin in the distribution of the ophthalmic branch of the trigeminal nerve (vascular malformation of skin), glaucoma, and leptomeningeal angiomas. Central nervous system abnormalities may increase the risk of hypothalamic-pituitary dysfunction. One previous study showed that SWS patients had higher prevalence of growth hormone deficiency than the general population although the etiology is unclear. This case report describes a patient who was initially diagnosed with SWS and later confirmed with complete growth hormone deficiency.

Case: A 7-year-and-11-month-old boy who had been diagnosed with SWS visited a tertiary center for the