PCP Handout

Caring for Persons with Klinefelter Syndrome

Klinefelter syndrome is a condition in which there is at least one Y chromosome and multiple X chromosomes, most commonly 47 XXY. Nondisjunction of oogenesis (40-50%) or spermatogenesis (50-60%) are most likely causes. Karyotype testing shows XXY in 90%, mosaicism in ~10% or smaller number with multiple extra sex chromosomes. There is some association with older parental age. Incidence estimates it affects ~1 in 660 males but a high percentage go undiagnosed with over 50% not diagnosed until adulthood.

System	Information	Follow up
Cognition	▪ 40% speech delay, > 75% some learning disability (math and complex language processing issues are common), ADHD/attention and executive function issues. ▪ Estimate each extra X chromosome lowers IQ 15 points	▪ Review psychometric testing, school assistance, ▪ consider decision making & caregiver needs
Cardio-vascular	▪ Anomaly 10-15%, most common patent ductus arteriosus, or atrial septal defect ▪ Increased risk diastolic dysfunction, mitral valve prolapse, shorter QT, increased atherosclerotic disease risk ▪ Increased varicose veins (20%) ▪ Leg ulcers (13%) assoc. with platelet hyperaggregability ▪ Increased risk venous thromboembolism	▪ Echocardiogram as indicated ▪ Exam LE skin/vascular status ▪ Consider VTE prophylaxis for high-risk events, i.e. surgery, central lines ▪ Testosterone may further increase VTE risk
GU	▪ Testicular degeneration begins in childhood, accelerates as adult. ▪ Infertility with oligo- or in most azoospermia, small adult testes, sperm retrieval rates 43-45% by TESE. ▪ Rare cryptorchidism, smaller penis 10-25% ▪ Inguinal hernias	▪ Infertility is often presenting symptom. ▪ Counsel re: assisted reproductive technologies, testicular sperm extraction (TESE) or microscopic TESE. Delay testosterone Rx until after extraction.
Endocrine	▪ Hypergonadotropic hypogonadism, delayed puberty 50%, ▪ Gynecomastia 20-33%, 50-75% increased breast tissue ▪ Increased abdominal fat mass, lower muscle mass ▪ 60-80% lack facial hair, 30-60% lack pubic hair ▪ Osteoporosis 10%, osteopenia 10-40% ▪ Fatigue from low testosterone. ▪ ~50% metabolic syndrome, diabetes mellitus 10-39%, thyroid disease rare	▪ Abnormal LH/FSH typically start around age 14. ▪ Low to low normal testosterone, test early morning x 2. ▪ Testosterone management – start with transdermal for dose adjustment, later IM method. ▪ On tx, testosterone, gonadotropins, hematocrit at least annually. Watch for polycythemia. ▪ Baseline dexa scan, periodic 2-10 year follow up
Musculo-skeletal	▪ 30% tall stature, especially long legs, narrow shoulders, wider hips ▪ Increased scoliosis, kyphosis, pectus excavatum/ carinatum, radio-ulnar synostosis, clinodactyly, pes planus ▪ increased autoimmune disease: SLE, Sjogren, RA	▪ Consider diagnosis in classic habitus and other signs, as currently highly undiagnosed
ENT	▪ High arch palate, hypertelorism ▪ Dental taurodontism (larger pulp, less enamel), premature dental decay 40%	▪ Maintain regular dental care
Oncology	▪ Inc. germ cell tumors: gonadal, mediastinal, retroperitoneal ▪ Inc. breast cancer: ~30x usual male risk ▪ Inc. non-Hodkin lymphoma, ? inc. lung cancer	▪ Regular testicular and breast exams ▪ Educate on self-monitoring ▪ Testosterone contraindicated in prostate cancer, consider screening
Psych	▪ Increased rates of mental illness: anxiety, depression ▪ Increased rates of gender dysphoria	▪ Screening and counseling referrals

References: (1) Rogol AD, et al. Klinefelter Syndrome. BMJ Best Practice June 2024.

(2) Sadri H. Klinefelter Syndrome: Identifying, characterizing & managing an underdiagnosed condition with serious consequences. Association for X&Y Variations, https://genetic.org/ Oct 2020.

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