

Objective:

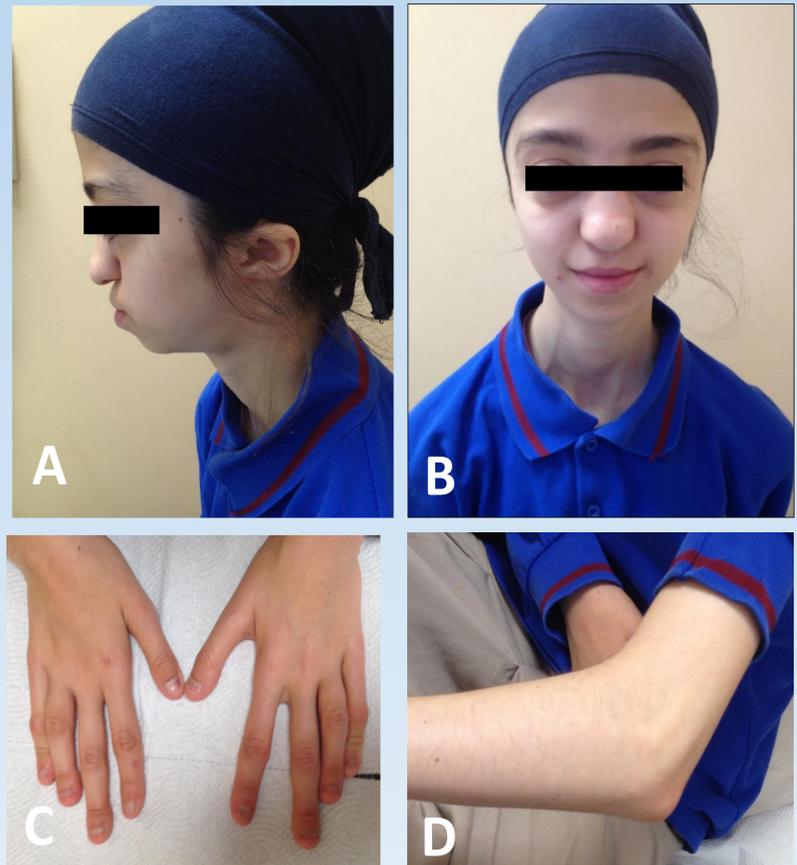
Antley-Bixler syndrome Type 1 (ABS1) is a rare form of craniosynostosis characterized by multiple craniofacial dysmorphic features, radio-humeral synostosis and urogenital abnormalities due to P450 oxidoreductase (*POR*) gene mutations. ABS is also associated with adrenal and gonadal failure which are sometimes underrecognized due to predominance of skeletal findings in various clinics. We report a female patient with very characteristic skeletal and facial features of ABS due to a homozygous *POR* mutation. Her diagnosis has been established while evaluating the etiology of primary amenorrhea at 16 years of age.

Case Report:

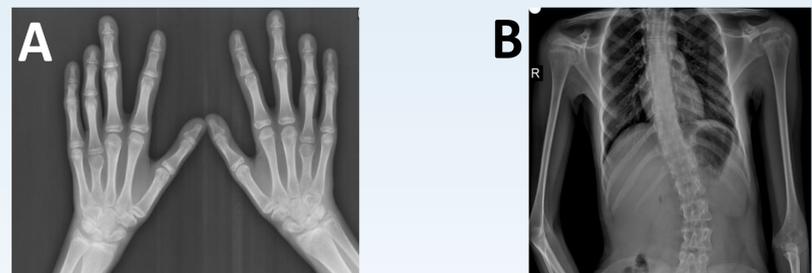
A sixteen years old girl was referred to our clinic for primary amenorrhea. She was born to parents from close villages at 39 weeks gestation with a birth weight of 3400 gr. The pregnancy was normal, and no virilization of the mother was mentioned. She was diagnosed with nephrocalcinosis in 2008 and recurrent urinary tract infections were noted. At presentation, facial dysmorphism including retro-micrognathia, high arched palate, and low-set deformed ears (Picture 1) and multiple skeletal abnormalities such as bilateral radio-humeral synostosis, hallux longus, arachnondactyly, shortening of the fourth metatarsal bones, pes planus, kyphoscoliosis, bilateral elbow dysplasia, were observed (Picture 2). Laboratory investigations showed high FSH (21.5 mIU/ml), LH (12.6 mIU/ml) and progesterone (38.9 ng/ml) levels, and, normal thyroid function test with low-normal sodium (135 mmol/L) and normal potassium (4.5 mmol/L) levels. Ultrasonography revealed normal uterus and ovaries but 6 mm nephrocalcinosis in the right kidney. High dose synacthen test revealed an exaggerated 17-hydroxyprogesterone, progesterone and a blunted cortisol response. Urinary steroid profiling by gas chromatography-mass spectrometry (GC-MS) revealed a unique steroid metabolome suggestive of *POR* deficiency (Picture 3). Hydrocortisone and combined estrogen and progesterone treatments were initiated. *POR* gene sequencing revealed a homozygous c.859G>C (p.A287P) mutation (Fluck CE, et al. Nat Genet. 2004;36:228-30).

Conclusion:

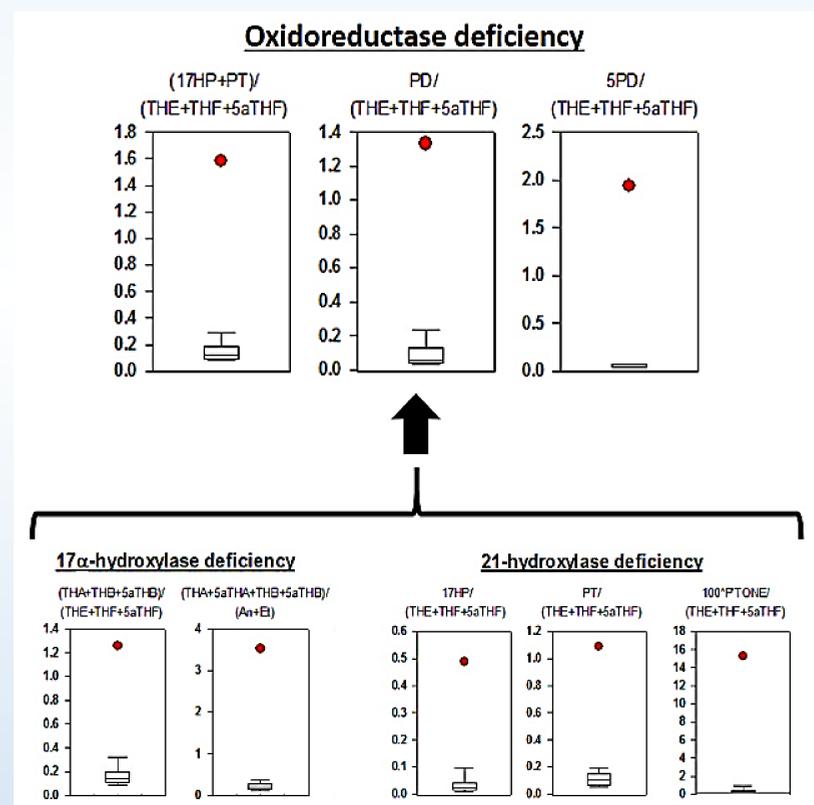
ABS should be kept in mind in the differential diagnosis of skeletal dysplasia. Impaired adrenal and gonadal steroidogenesis are important considerations for the clinicians dealing with ABS for early diagnosis and treatment.



Picture 1. A – B) Lateral and front views of patient, C) Arachnodyly, shortening of the fourth metatarsal bones D) Radio-humeral synostosis



Picture 2. A) Hypoplasia of 3rd and 4th distal phalanges, dysplasia of 5th middle phalanx, shortening of bilateral 4th metacarpals, B) Kyphoscoliosis



Picture 3. Urine steroid profiling by gas chromatography-mass spectrometry showing low excretion of glucocorticoid and androgenic metabolites

Acknowledgement: GC-MS work has been done in Wiebke Arlt's lab.