Pharmacotherapy: The Food, and Drug Administration [FDA] has approved several drugs for long term weight management, for example, Orlistat, Lorcaserin, Liraglutide, Phentermine-topiramate, and naltrexone-bupropion.[3] They each have a different mechanism of action, and have additive effect in conjunction with restricted calorie diet and increased physical activity. The side effects of these drugs are well studied, and long term usage of drugs such as phentermine [beyond the FDA approved duration] is discouraged.[15] Metreleptin (a recombinant leptin analog) has been used in leptin deficiency.[16]

***LEPR*:** The *LEPR* gene encodes for a protein belonging to the gp130 family of cytokine receptors. It is the receptor for leptin. Six isoforms of this receptor have been identified, but only the longest (ObRb) has full signaling ability. It is expressed on the surface of cells in many organs and tissues of the body, including the hypothalamus. Leptin binds to the leptin receptor, and initiates a cascade of various signal transduction pathways. Activation of the Jak2 and STAT3 pathway leads to an increase of anorexigenic [loss of appetite] signals, and a decrease of orexigenic [appetite stimulant] signals.[17] Mutations in leptin receptor entails presence of less receptor protein at the cell surface. Even if leptin binds to such receptors, their signaling is disrupted/impaired.[17] Excessive hunger, massive weight gain, and reduced production of hormones that direct sexual development (hypogonadotropic hypogonadism) are the resulting sequelae.

The patient was detected with a homozygous *LEPR* c.1055G>A, p.(Cys352Tyr) variant, which is classified as likely pathogenic. Its cytogenetic location is: 1p31.3. The transcript NM_001003680.3 encodes for a missense mutation [i.e. a point mutation results in a codon that encodes for a different amino acid]. Its associated phenotype is leptin receptor deficiency, and its inheritance pattern is autosomal recessive [i.e. two copies of an abnormal gene must be present in order for the disease or trait to develop]. The variant was confirmed using bidirectional Sanger sequencing. Not only does this inspire confidence in reporting, but it also establishes the mutation specific test for screening family members.

Mutation in *LEPR* was first described by Clément et al. (1998).[18] They reported homozygosity for a mutation in the *LEPR* gene, a G-to-A transition at the +1 position of intron 16. Farooqi et al. (2007)[19] sequenced *LEPR*, and evaluated metabolic, endocrine, and immune functions in 300 subjects with severe early onset obesity. Ninety of these probands were from consanguineous families. They reported 8 (3%) cases with nonsense, or missense mutations in *LEPR*, leading to impaired receptor signalling. BMI standard-deviation score for these probands