completely normal hormonal analysis, although the patient reported by Griesinger et al. displayed hyperandrogenism (1). Although these two cases are extremely rare examples of MRKH syndrome associated with TAR syndrome, they pose an interesting relationship between the development of the limb buds and the müllerian ducts.

Alex J. Childs, M.D.
Lori-Linell H. Hall, M.D.
Division of Reproductive Endocrinology and Infertility
Department of Obstetrics and Gynecology
Memorial Health University Medical Center
Savannah Campus, Mercer University School of Medicine
Savannah, Georgia
March 19, 2005

REFERENCES

Reply of the Author:
I believe the short case report by Drs. Childs and Hall is certainly a relevant addendum to our case report and is worth publishing. However, there are no specific comments I would have to add in reply to the letter of Dr. Childs.

Georg Griesinger, M.Sc.
Klinikum für Frauenheilkunde und Geburtshilfe
Universitätsklinikum Schleswig-Holstein, Campus Lübeck
Luebeck, Germany
April 4, 2005

Editorial Commentary
Hot clues to the etiology of Mayer-Rokitansky-Küster-Hauser syndrome?

The Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome is characterized by congenital absence of the vagina, with bilateral nonfunctional rudimentary uteri. The MRKH syndrome is frequently associated with anomalies of the urinary tract, skeleton, and less frequently with cardiac defects. Ovarian function is normal, and the karyotype of the patients is always 46,XX. The authors describe the association of the Mayer-Rokitansky-Küster-Hauser syndrome with thrombocytopenia-absent radius syndrome (TAR). The report by Griesinger et al. is not the first time that the Mayer-Rokitansky-Küster-Hauser syndrome has been described in association with various types of rather well-delineated skeletal dysplasias (1). The association of MRKH syndrome with the Klippel-Feil syndrome has been known for quite a while, and the association with Holt-Oram syndrome (HOS) was recently described for the second time by Ulrich et al. (2, 3).

Holt-Oram syndrome is characterized by congenital heart abnormalities and skeletal malformations of the upper limb. Most importantly, the gene for HOS has been isolated and mapped to the long arm of chromosome 12(12q24.1). The Holt-Oram gene encodes a T-box containing transcription factor, referred to as TBX5. The overlap between the skeletal features of the MRKH syndrome, the Klippel-Feil syndrome, HOS, and the TAR syndrome is remarkable. Given the isolation of the gene for HOS, it might be a good idea to look for mutations in TBX5 in all of these syndromes. Cervicothoracic somite dysplasia is a common feature of all four syndromes.

There are several other reports in which vaginal atresia is observed in association with skeletal anomalies (4). These reports suggest that it might be rewarding to search the TBX group of transcription factors rather than genes related to sexual development. The recent report of a WNT4(1p31-p35) missense mutation in a patient with MRKH syndrome and questionable androgen overproduction seems to be stretching a point to bring the human phenotype closer to the features observed in female mice with mutant wnt4 (5).

Paul G. McDonough, M.D.
Associate Editor, Letters
Department of Obstetrics and Gynecology
Medical College of Georgia
Augusta, Georgia
Received April 9, 2005.

REFERENCES
doi:10.1016/j.fertnstert.2005.04.014