

Involvement of ADAMTS-1 in folliculogenesis, ovulation, and organization of the medullary vascular network in the ovary

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ADAMTS-1 null mice displayed renal anomalies involving enlarged calices and atrophic renal papillae, which resemble ureteropelvic junction (UPJ) obstruction in humans. We also found that ADAMTS-1 null female mice were infertile, indicating that ADAMTS-1 is important for the function of female reproductive organs. To clarify the role of ADAMTS-1 in ovarian function, we examined abnormalities in the ovulatory processes, folliculogenesis, and the vascular system of ADAMTS-1 null ovaries.

First, when immature female mice were treated with pregnant mare serum gonadotropin (PMSG)/human chorionic gonadotropin (hCG), the number of ovulated oocytes was markedly decreased in ADAMTS-1 null mice when compared with ADAMTS-1 (+/-) controls. The proportion of anovulated follicles to total mature follicles was significantly higher in ADAMTS-1 null females when compared with controls. The numbers of growing follicles at each stage were counted. The number of follicles at type 5b (late preantral) and later stages was markedly reduced in ADAMTS-1 null mice, irrespective of gonadotropin treatment. These data demonstrate that impairment of ovarian function to ovulate oocytes in ADAMTS-1 null mice occurs at two different levels: in the development of growing follicles and in ovulatory processes. Furthermore, ADAMTS-1 null ovaries was found to include a number of unusual atretic follicles that showed no sign of oocyte degeneration but that had lost the surrounding granulosa cell layers and were considered to be derived from type 4 or 5a follicles. These results suggest that ADAMTS-1 is important for follicular development beyond the type 4 and/or 5a and for maintaining normal granulosa cell layers in follicles. Finally, the number of large blood vessels in the medullar zone was significantly decreased in ADAMTS-1 null mice ovaries, suggesting that ADAMTS-1 is also involved in the organization of the medullary vascular network in the ovary.

