As one of the most rapidly evolving proteins of the genus *Betacoronavirus*, ORF8's function and potential pathological consequence *in vivo* are still obscure. In this study, we show that the secretion of ORF8 is dependent on its N-terminal signal peptide sequence and can be inhibited by ROS scavenger and ER-Golgi transportation inhibitor in cultured cells. To trace the effect of its possible *in vivo* secretion, we examined the plasma samples of COVID-19 convalescent patients and found that the patients aged 40 to 60 had higher antibody titers than those under 40. To explore ORF8's *in vivo* function, we administered the mice with ORF8 via tail-vein injection to simulate the circulating ORF8 in the patient. Although no apparent difference in body weight, food intake, and vitality was detected between vehicle- and ORF8-treated mice, the latter displayed morphological abnormalities of testes and epididymides, as indicated by the loss of the central ductal lumen accompanied by a decreased fertility in five-week-old male mice. Furthermore, the analysis of gene expression in the testes between vehicle- and ORF8-treated mice identified a decreased expression of Col1a1, the loss of which is known to be associated with mice's infertility. Although whether our observation in mice could be translated to humans remains unclear, our study provides a potential mouse model that can be used to investigate the impact of SARS-CoV-2 infection on the human reproductive system.