

Exaggerated placental site is a benign, nonneoplastic lesion characterized by an increased number of implantation-site intermediate trophoblastic cells that extensively infiltrate the endometrium and underlying myometrium. An exaggerated placental site may occur in association with normal pregnancy or an abortion. In the past, this lesion was designated syncytial endometritis, but recently the term *exaggerated placental site* was introduced by the World Health Organization because the lesion is not inflammatory or confined to the endometrium and most of the constituent cells are not syncytial. An exaggerated placental site is composed of implantation-site intermediate trophoblastic cells, which display an identical immunophenotypic profile to the intermediate trophoblastic cells found in the normal implantation site, supporting the view that this lesion is an exaggeration of a normal physiologic process.

Morphologic Features

The exaggerated placental site is defined as an increased number of implantation-site intermediate trophoblastic cells exceeding those normally present in the implantation site. Based on a review of the surgical pathology files at the Johns Hopkins Hospital, it occurs in approximately 1.6% of spontaneous and elective abortions from the early first trimester. The lesion is composed predominantly of mononucleate implantation-site intermediate trophoblastic cells and variable numbers of multinucleated intermediate trophoblastic cells that extensively infiltrate the endomyometrium. Despite the extensive infiltration by intermediate trophoblastic cells, the overall architecture of the implantation site is not disturbed. Endometrial glands may be completely surrounded by trophoblastic cells but are not destroyed, and similarly the smooth muscle cells of the myometrium are separated by cords, nests, and individual implantation-site intermediate trophoblastic cells that diffusely infiltrate the myometrium without producing necrosis. The surrounding decidua, however, may show degeneration and necrosis typical of spontaneous abortion. Other features associated with gestation are usually present including hyalinized spiral arteries, hypersecretory glands, and chorionic villi. Despite the profuse infiltration of trophoblastic cells, the Ki-67 index of these cells is near zero, suggesting that the increased number of trophoblastic cells is not the result of *de novo* proliferation in the implantation site.

Differential Diagnosis

At times, an exaggerated placental site may be difficult to distinguish from a placental-site trophoblastic tumor (PSTT), particularly in curetting, as the diagnostic criteria for an exaggerated placental site are imprecise. There are no reliable data quantifying the amount and extent of infiltration of implantation-site intermediate trophoblast at different stages of normal gestation. Besides the overlap in the morphologic features of exaggerated placental site and PSTT, trophoblastic cells in early gestation have a primitive appearance and invade the uterine wall and spiral arteries extensively, thus invalidating the conventional histologic features used to distinguish a benign from a malignant process. The exaggerated placental site is microscopic, lacks mitotic activity, is composed of intermediate trophoblastic cells separated by masses of hyaline, and usually is admixed with decidua and chorionic villi. In contrast, a lesion unaccompanied by villi and composed of confluent masses of implantation-site intermediate trophoblastic cells

that display unequivocal mitotic figures is classified as a PSTT. In addition, multinucleated trophoblastic cells are more often present in an exaggerated placental site than in a PSTT.

Recent studies show that the Ki-67 nuclear labeling index using a Ki-67-specific (MIB-1) antibody is superior to the mitotic index as a diagnostic aid in the differential diagnosis of exaggerated placental site versus PSTT. Specifically, the Ki-67 index (mean \pm standard deviation) of the trophoblastic cells in an exaggerated placental site is near zero in contrast to $14\% \pm 6.9\%$ in a PSTT. Because Ki-67 labeling may occur in the lymphoid cells normally present at the placental site, it is important to be certain that Ki-67 labeling is assessed only in an intermediate trophoblast using strict cytologic criteria. In difficult cases, double immunostaining utilizing an antibody against Mel-CAM or HLA-G that specifically defines implantation-site intermediate trophoblastic cells, can assist in this distinction. For further inquiry about the Mel-CAM and HLA-G antibody, please contact Dr. Shih (E-mail address: ishih@jhmi.edu).

Behavior and Treatment

An exaggerated placental site is a benign trophoblastic lesion that involutes following curettage. It does not include the exaggerated placental site-like implantation site associated with moles, and it is not associated with increased risk of persistent gestational trophoblastic disease. No specific treatment or follow-up is necessary. When an exaggerated placental site cannot be confidently distinguished from PSTT by morphology and immunohistochemistry, close follow-up with serial hCG titers is advisable.