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RESEARCH ARTICLE

Association between Chronic Inflammation of Basal Plate and Decidua Existences with Placenta Accreta Spectrum

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Abstract

The placenta accreta spectrum (PAS) is an abnormal placenta condition with a high level of morbidity and mortality in both the mother and fetus. The PAS has a multifactorial etiology, one of which is a chronic inflammation of the basal plate (CIBP) and the decidual existences (DE). The study aims to analyze the association between CIBP and DE with PAS. It was an analytical observational with a cross-sectional study design on 50 placentae (25 PAS paraffin block, 25 standard placenta samples) from Dr. Hasan Sadikin General Hospital and other health centers that meet the inclusion and exclusion criteria. The data are taken from PAS patients from January 2015–December 2020. All samples will be stained with hematoxylin-eosin (HE), then undergo histopathological examination. The result of the studies analyzed statistically using Fisher's exact. CIBP in PAS was found in 21/25 cases, while in the normal placenta was found in 16/21 patients. The DE is positive in 15/25 cases of PAS, whereas the normal placenta was found in all cases. The association between CIBP and PAS is insignificant statistically (p=0.19), while the DE showed a significant relationship with PAS (p=0.00). The presence of the decidua is related to the regulation of trophoblastic invasion into the myometrium in PAS cases. CIBP can occur due to the reaction of decidua tissue to trophoblastic invasion or an infectious agent. The pathogenesis of PAS needs further understanding so that the appropriate therapy can be found for its prevention and management.

Keywords: Decidua, inflammation, placenta accreta spectrum

Introduction

The placenta accreta spectrum is defined as an abnormal attachment of the placenta to the myometrium with the varying invasion of trophoblastic. It is divided into three categories: 1) the attachment of the trophoblastic into the surface of the myometrium (placenta accreta), 2) trophoblastic invasion into the myometrium (placenta increta), 3) trophoblastic invasion through the entire thickness of the myometrium from the serous layer to the surrounding intraabdominal organs (placenta percreta).[1,2]

PAS has increased tenfold worldwide in the last 50 years,[3–5] showing an incidence of 3 in 1,000 pregnancies in the previous ten years.[3] The PAS causes significant morbidity and mortality associated with postpartum hemorrhage.[4,5] Wu et al.[6] reported an increase in the incidence of PAS from 1:2,150 in 1994 to 1:533 in 2005. However, this incidence has increased to three per 1000 births in the last decade and is in line with the increasing rate of cesarean sections.[3,7–9]

Maternal morbidity on PAS is reported to reach 60%, including hysterectomy, the need for blood transfusion, and prolonged stay with mortality exceeding 7%. In addition, the incidence of perinatal complications is increasing due to premature birth, low birth weight, and inadequate gestational period, which increases the need for neonatal intensive care unit (NICU) and resuscitation.[10–12]

The PAS is a multifactorial process. The underlying molecular mechanism is not widely known. Several hypotheses regarding the formation of PAS reveal that the disorder's pathogenesis is caused by a decidual defect and excessive invasion of trophoblast cells into the myometrium.[13] The underlying etiology is not clearly understood. Still, interactions between decidua tissue on the basal lamina, inflammatory cells, and extravillous trophoblast cells (EVT) are thought to be involved in developing PAS. Several studies have reported the relationship between pathological conditions on the basal plate and PAS.[14]

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Prior studies have shown that PAS is formed due to the failure of normal decidua formation, an endometrial defect, or a failure that changes the endometrium to decidua. In the absence of the typical decidua plate and Nitabuch layer, the villous trophoblast has direct access to the myometrium. Trophoblast migration and infiltration during normal placental development are affected by autocrine or paracrine behavior by various types of molecules such as growth factors and their receptors, cytokines, hormones, adhesion molecules, and enzymes. The decidua existence is thought to prevent abnormal placental formation by providing autocrine or paracrine regulation.[15,16]

This study is focused on examining the association between chronic inflammation of the basal plate and decidua existences with PAS.

Methods

This research was an analytical observational study with a cross-sectional study design. The subjects of this study consisted of 50 placental samples (25 samples in the form of PAS paraffin blocks, 25 samples from normal pregnancies) from Dr. Hasan Sadikin General Hospital and other health centers that meet the inclusion and exclusion criteria. The data are taken from PAS patients from January 2015–December 2020. Data collection was carried out after an ethical review was received. The characteristics of the research subjects were obtained from patient's medical records, using purposive sampling as its research sample method. Tracing was done to placental paraffin blocks of patients with PAS, then underwent histopathological preparations in Dr. Hasan Sadikin Hospital Bandung. Meanwhile, placentas obtained from normal pregnancies as controls were prepped into paraffin blocks and histopathological preparations in the Clinical Laboratory of Universitas Islam Bandung. All samples were stained with hematoxylin-eosin (HE) and were examined histologically to assess the presence of decidua and chronic inflammation on the basal plate using an Olympus CX 21 LED light microscope at 200× and 400× magnification. Histopathological assessment was performed double-blind by two anatomical pathologists. Data of this study will be analyzed statistically using Fisher's exact to determine the association between the two variables. This study received its ethical approval from the Research Ethics Committee of Universitas Padjadjaran with the number 777/UN6.KEP/EC/2021.

Results

The numbers of patients were 25 patients who had been diagnosed histopathologically with placenta accreta, increta, and percreta. Placenta accreta is characterized by the attachment of chorionic villi to the myometrium without interference by the decidua or fibrinoid tissue. In contrast, placenta increta is diagnosed when the chorionic villi infiltrate the myometrium. Placenta percreta is defined as the presence of chorionic villi infiltration throughout the thickness of the myometrium or serous layer (Figure 1). In addition, the placentas from patients with uncomplicated pregnancies collected from 25 patients from various hospitals were used as controls.

In this study, observations under the microscope were made on all samples. The Table presents data from histopathological examination to assess the presence of decidua and chronic inflammation of the basal plate on hematoxylin-eosin stained PAS and normal placentas.

The Table shows that basal plate inflammation in PAS is found in 21/25 cases. Decidua basalis is found in 15 cases of PAS in this study. Sixteen cases had signs of inflammation of the basal plate in the normal placenta, while all cases with normal pregnancies show the presence of decidua. The table above shows an insignificant association between basal plate inflammation and PAS statistically, while the decidua existences had shown statistical significance with PAS. The ratio of the presence of decidua in the PAS group is significantly different, with p=0.00.

Discussion

In this study, CIBP in PAS (Figure 2) did not significantly differ from normal pregnancies. Chronic inflammation of the placenta can be caused by cytomegalovirus, *Toxoplasma gondii*, and *Treponema pallidum*, although most chronic inflammation lesions are proven caused by non-infectious factors.[17] Chronic inflammation of decidua (deciduitis) is diagnosed by the presence of lymphocytes and plasma cells in the basal plate that has an incidence of 1–4% of unknown etiology. In this study, CIBP in PAS may represent an immune response at the fetal and maternal interface. It may be found as a basal plate reaction

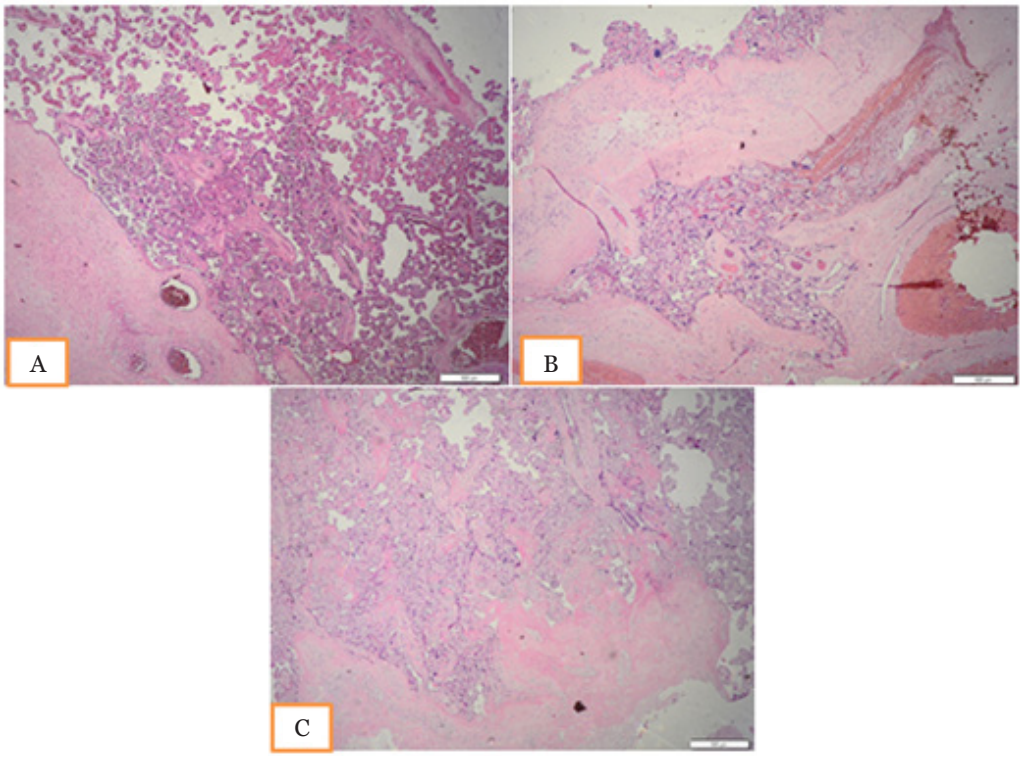

Figure 1 Histopathological Appearance of Placenta Accreta Spectrum
Hematoxylin-eosin staining, 100× magnification. (**A**) Placenta accrete. (**B**) Placenta increate. (**C**) Placenta percreta

to trophoblastic tissue invasion that plays a role in controlling its invasion.[18,19] Ernst et al.[18] suggested when PAS is identified; the placenta is more often affected by chronic inflammation of the basal plate, altered maternal vascular malperfusion, and subchorionic/intervillous hemorrhage. Several research found a close relationship between the microenvironment of PAS and tumor behavior. Both conditions require the ability of cells to defend local immunological systems, trophoblast invasion activity, and angiogenesis.[19]

Successful pregnancies depend on fetoplacental mediated suppression of the host immune response to prevent maternal rejection. Chronic inflammation of the basal plate is associated with PAS incidence. The significance of the leukocyte subpopulations and their

Table Association between Chronic Inflammation of Basal Plate and Decidual Existences with Placenta Accreta Spectrum

Criteria	Placenta		Total (n=50)	p*
	PAS (n=25)	Normal (n=25)		
Chronic inflammation basal plate				
Negative	4	9	13	0.190
Positive	21	16	37	
Decidual existences				
Negative	10	0	10	0.000
Positif	15	25	40	

Note: PAS: placenta accreta spectrum; *Fisher's exact

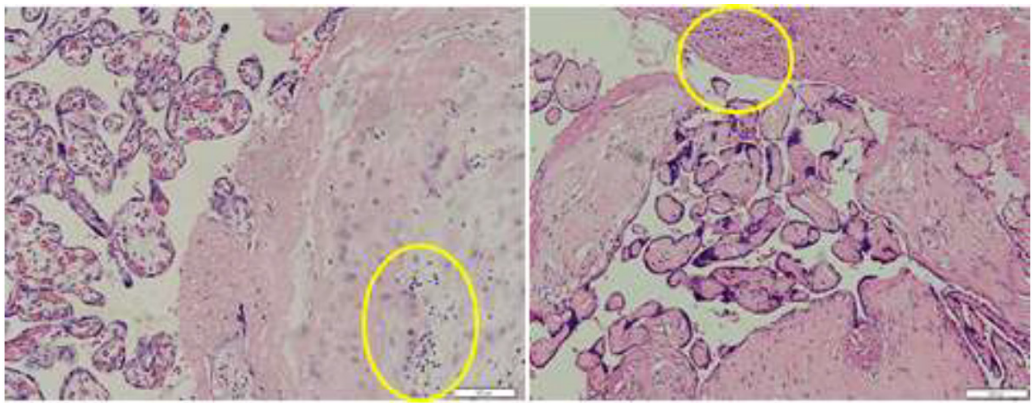

Figure 2 Chronic Inflammation of the Basal Plate
Hematoxylin-eosin staining, 200× magnification

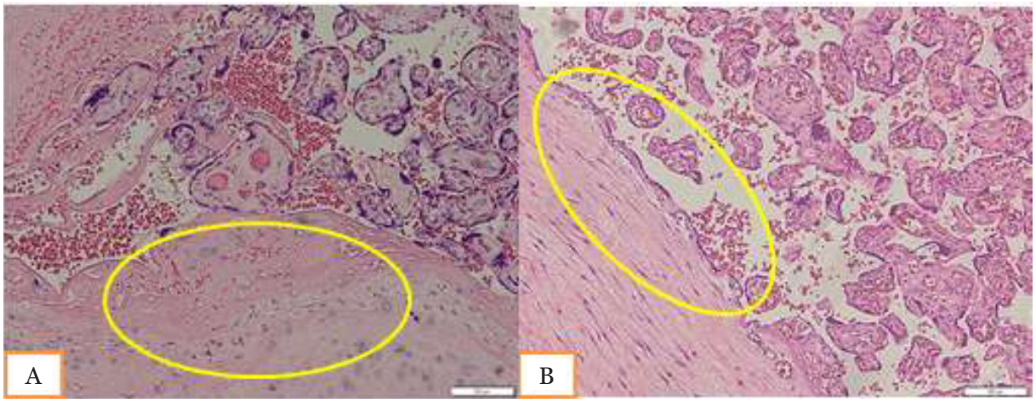

Figure 1 (A) Decidual Existences (Yellow Circle). (B) Chorionic Villi Attached Directly to the Myometrium without Decidua (Yellow Circle)
Hematoxylin-eosin staining, 200× magnification

contribution to EVT over-invasion in PAS requires further investigation. Ernst et al.[18] demonstrated an increase in lymphocyte infiltration at the implantation site of PAS specimens compared with patients with placental malignancies without clinical suspicion of PAS.

Lymphocytes are known to participate in placental implantation and remodeling of the blood vessels. Decidual natural killers (NK) are inflammatory cells that regulate placenta implantation and the spiral arteries' remodeling process.[16,20] Laban et al.[16] report the role of NK cells in PAS development. The decrease in the NK cell population was closely related to PAS incidence. Nevertheless, increased NK cells may give protection effects against EVT invasion. Plasma cells are not a normal component of the endometrial stroma, and the accumulation of these cells indicates the abnormal condition of the endometrium.

The local uterine injury (e.g., previous cesarean section) could result in impaired decidualization/local scarring and abnormal placental attachment in subsequent pregnancies that correlates with PAS cases. Although it is associated with the cesarean delivery history, even a minor disruption of the uterine lining can cause subsequent placenta accretion.[21–23]

In this study, most cases of PAS showed the presence of decidua (Figure 3). It is characterized by direct contact between the chorionic villi and the underlying myometrial structure histopathologically.[19] However, some studies reported that decidua is still found around the

trophoblast invasion in 44–69% of cases of PAS.[23] Microscopic examination of the placenta also confirms the presence of placental basal plate myometrial fibers, although these findings may be seen in a normal pregnancy. Their presence indicates an abnormal separation of the placenta from its place.[24] Hannon et al.[14] reported the absence of local decidua was associated with a more significant number of interstitial EVTs—rather than endovascular EVTs involved in spiral artery remodeling—that invaded the myometrium with less multinucleated trophoblast giant cells (MTGC) formation. The capacity of MTGC is associated with the cessation of trophoblast invasion into the myometrial wall.

During normal pregnancy, EVT invades the myometrium's decidual and inner third layer. Invasion occurs through two pathways; interstitial EVT invades the decidua from anchoring villi and cytotrophoblasts, whereas endovascular EVT arises from an intravascular invasion of transmural migration of interstitial EVT into spiral arteries lumens to change the endothelial cells. Terminal differentiation of the EVT, with the formation of MTGC in the decidua and inner third of myometrium, will restrain trophoblast invasion of the myometrium. In PAS cases, abnormal EVT invasion is found, and the number MTGCs has been reported to be reduced. However, these findings are inconsistent in several studies.[12]

There was some weakness in this study, including the limited number of samples and not including several clinical data/patient characteristics that may contribute to the study results. In addition, this study still uses the assessment/evaluation of the existence of the decidua using the HE staining. Therefore, it is needed to conduct further research to evaluate the association between chronic inflammation of the basal plate and the decidua existences by using immunohistochemically staining with a more significant number of samples.

Conclusion

The decidua existences in placental preparation are relevant significantly with the PAS, whereas the signs of chronic inflammation of the basal plate did not provide a significant association.

Conflict of Interest

None declared.

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