Int J Clin Exp Pathol 2016;9(7):7237-7243
www.ijcep.com /ISSN:1936-2625/IJCEP0025339

Original Article

Placenta percreta with small bowel invasion: unusual presentation of abnormal placental adherence

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Received January 31, 2016; Accepted May 20, 2016; Epub July 1, 2016; Published July 15, 2016

Abstract: Abnormal adherence of the placenta to the myometrium can lead to failure of normal postpartum placental separation. Owing to increasing rates of cesarean section, the incidence of morbidly adherent placenta has increased. Abnormally adherent placenta is classified according to its degree of invasion of the myometrium. When the placenta penetrates completely through the myometrium, it may result in placenta percreta, possibly involving adjacent structures or organs such as the urinary bladder or rectum. The urinary bladder is the most commonly affected pelvic structure, whereas the involvement of other abdominal organs by placenta percreta is an extremely rare condition. We describe a rare case of placenta percreta invading the terminal ileum and mesentery. A 40-year-old woman presented at 28 weeks of gestation with irregular uterine contraction and vaginal bleeding. She underwent a repeat cesarean section and explorative laparotomy. Segmental resection of the perforated terminal ileum was performed. Histopathological examination revealed an adherent placenta with invasion of the chorionic villi into the ileal subserosa and mesentery. The trophoblastic origin was confirmed by immunohistochemistry. Placenta percreta is associated with high maternal mortality and morbidity rates, mostly secondary to intraoperative bleeding and its consequences. A high index of suspicion for placenta percreta is required when evaluating pregnant women with a prior history of cesarean section. Ultrasonography and magnetic resonance imaging may assist in establishing the diagnosis preoperatively. With proper planning and a multidisplinary approach, fetal and maternal morbidity and mortality may be decreased.

Keywords: Abnormally adherent placenta, placenta percreta, small bowel, perforation

Introduction

Abnormal adherence of the placenta to the myometrium can lead to failure of normal postpartum placental separation [1]. Abnormally adherent placenta is classified according to its degree of invasion into the myometrium [2]. When the chorionic villi are attached to the myometrium without invasion but placental separation is difficult, it is classified as placenta accreta. When partial myometrial invasion occurs, it is classified as placenta increta. When the placenta penetrates completely through the full thickness of the myometrium, it is classified as placenta percreta that possibly involves adjacent structures. Predisposing risk factors include uterine scarring usually due to previous cesarean sections, endometrial curettage, previous placental retention requiring manual removal, and endometriosis [1]. With the increasing tendency of cesarean section and obstetric surgery, the incidence of abnormal placental adherence has been increased tenfold over the last 50 years [3, 4].

Normally, the placenta is attached to the upper uterine segment, occupying part of the fundus and passing down onto the anterior or posterior walls. The placental trophoblastic tissue does not normally invade the myometrium, as they are separated by the decidual plate. Abnormally adherent placenta is attributed to complete or partial absence of the decidual plate, allowing abnormal penetration of trophoblastic tissue into the myometrium. Placenta percreta, the severe form of abnormal placental adherence, rarely occurs but can result in fatal outcome such as uterine rupture and hemoperitoneum.

Table 1. Antibodies used for immunohistochemical staining

Antibody	Source	Clone	Dilution
hCG	Dako, Agilent Technologies, Inc., Carpinteria, CA, USA	Polyclonal	1:600
hPL	Dako, Agilent Technologies, Inc., Carpinteria, CA, USA	Polyclonal	1:400
Inhibin-α	AbD Serotec, Kidlington, Oxfordshire, UK	R1	1:50
p63	Dako, Agilent Technologies, Inc., Carpinteria, CA, USA	DAK-p63	1:150
CK	Dako, Agilent Technologies, Inc., Carpinteria, CA, USA	AE1/AE3	1:100

hCG: Human chorionic gonadotropin; hPL: Human placental lactogen; CK: Cytokeratin.

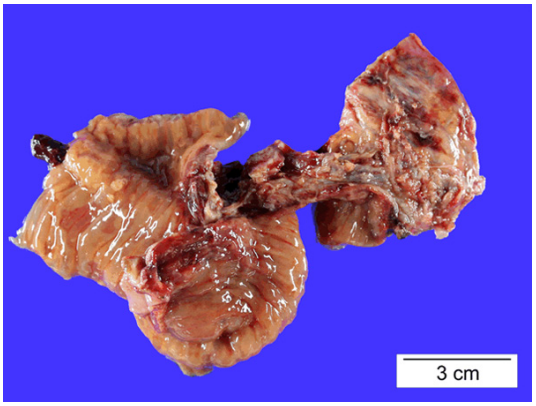

Figure 1. Gross findings of the resected terminal ileum. The mesenteric and serosal surfaces are covered with fibrinous exudates and blood clots. No placental tissue is grossly evident. The mucosal surface exhibits a few small areas of hyperemic and edematous changes, without evidence of neoplastic lesion.

Furthermore, the chorionic villi may extend to the adjacent organs or structures such as the urinary bladder or rectum. The incidence of placenta percreta with invasion of adjacent organs is low, but the most commonly affected pelvic structure is the urinary bladder. Placenta percreta is fatal because of the high risk of complications from secondary uterine rupture or adjacent organ involvement, and because of late diagnosis, often only discovered at the time of delivery. Complications occur when the anatomy of the lower uterine segment is distorted; and the massive blood vessels that often supply the placenta from the pelvic side wall are torn during manipulation, resulting in severe hemorrhage.

Placenta percreta rarely invades pelvic or abdominal organs other than the urinary bladder or rectum. Nevertheless, we recently encountered a rare case of placenta percreta with small bowel invasion in a 40-year-old woman who had a history of cesarean section due to placental abruption. The placenta percreta was not discovered during prenatal monitoring. When terminal ileum involvement of the placenta percreta was discovered during the repeat cesarean section, small bowel segmental resection was performed. In addition, we performed a thorough histopathological examination and immunohistochemical staining of the resected specimen.

Patient and methods

Case presentation

A 40-year-old woman (gravida 3, para 2) was referred to our institution at 28+1 weeks of gestation because of irregular uterine contractions. Her medical history did not indicate any medical problems. She had a history of one cesarean section. Her obstetric history indicated that 8 years prior, she had a vaginal delivery following an uneventful pregnancy course. Her second pregnancy was complicated by placental abruption with resultant fetal death. Physical examination demonstrated anemia and a uterine size consistent with the gestational period. Laboratory evaluation revealed a hemoglobin level of 9.8 g/dL, hematocrit level of 28.4, and normal coagulation profile and renal function. At 29+2 weeks of gestation (on the eighth day of hospital stay), the patient complained of severe abdominal pain and was taken to the operation room. She underwent a repeat cesarean section and exploratory laparotomy.

Histopathological examination

The resected specimen was fixed in 10% neutral-buffered formalin and was embedded in paraffin blocks. Four-micrometer sections were cut from each formalin-fixed, paraffin-embedded (FFPE) block and stained with hematoxylin and eosin, and prepared for immunohistochemical staining. All available slides were examined under routine light microscopy by two independent pathologists.

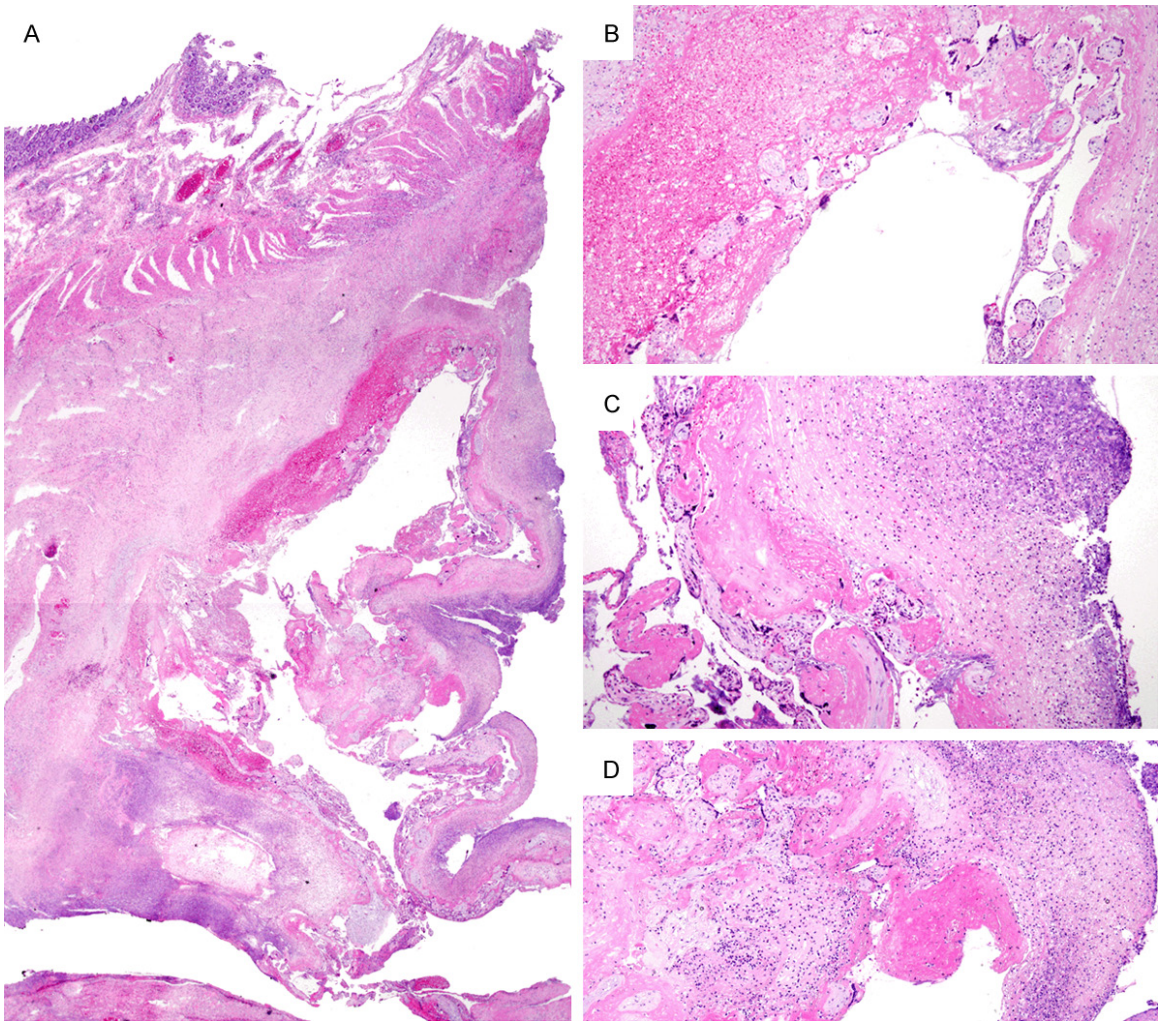

Figure 2. Histopathological findings. (A) The terminal ileum and mesentery show acute fibrinopurulent inflammatory infiltrates involving the ileal subserosa and serosa, whereas the mucosa, submucosa, and proper muscle appear intact. (B and C) At the serosal surface, the chorionic villi and syncytiotrophoblasts are admixed with fibrinoinflammatory exudates or associated with abscess. (D) Owing to extensive inflammatory response, a few chorionic villi underwent fibrinoid necrosis.

Immunohistochemical staining

Four-micrometer FFPE tissue sections were deparaffinized and rehydrated with a xylene and alcohol solution. Immunohistochemical staining was performed by using the Ventana Benchmark XT automated staining system (Ventana Medical Systems, Inc., Tucson, AZ, USA) or Dako Omnis (Dako, Agilent Technologies, Inc., Carpentaria, CA, USA) according to the manufacturer's instructions. Antigen retrieval was performed by using Cell Conditioning Solution (CC1; Ventana Medical Systems, Inc.) or EnVision FLEX Target Retrieval Solution, High pH (Dako, Agilent Technologies, Inc.). The tissue sections were subsequently incubated with primary antibodies (**Table 1**). After the chromogenic visualization step using the ultraView Universal DAB Detection Kit (Ventana Medical Systems, Inc.) or EnVision FLEX/HRP (Dako, Agilent Technologies, Inc.), slides were counterstained with hematoxylin and coverslipped. Appropriate positive and negative controls were stained concurrently to validate the staining procedure.

Results

Operative findings

Preoperative mechanical bowel preparation could not be performed. During opening of the

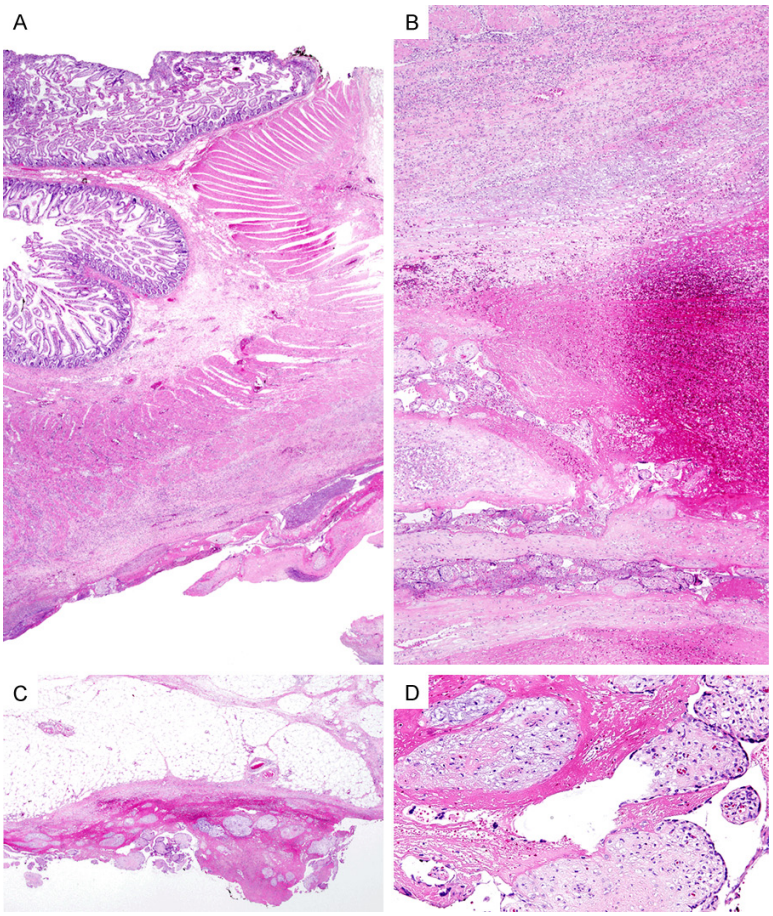

Figure 3. Histopathological findings of the chorionic villi invading the subserosa and mesentery. (A) In most areas, the chorionic villi just attached to the serosa. (B) However, in some areas, they form loose, irregularly shaped clusters and infiltrate the inflamed (B) subserosa and (C) mesentery. (D) The individual trophoblasts and villous stromal cells show neither cellular proliferation nor cytologic atypia. The villi show no significant edematous change.

abdominal wall, the field of view was limited due to severe adhesion. Immediately after peritoneal incision, the uterine wall ruptured, and a large volume of blood gushed out, along with some placental tissue discharged from the uterus. Then, immediately after the uterine wall was opened with an inverted-T incision, placental tissue measuring about one-fourth of the total placental volume and part of the thin umbilical cord were discharged. Subsequently, during fetal delivery, the fetus was confirmed to have a right shoulder presentation. This was assumed to be due to the oblique contour of the uterus caused by severe intrauterine adhesion resulting from the previous cesarean section. In addition, because the myometrium and placental tissue are highly friable, the possibility of an inflammatory lesion was suspected. After delivery of both the fetus and the placenta, the abdominal and pelvic cavity was observed in detail and the terminal ileum was confirmed to be severely adhered to the uterine fundus and anterior wall. More than one-half the total length of the terminal ileum was torn transversely. In addition, because the omentum was severely adhered to the small bowel, colon, uterus, and abdominal peritoneum, the posterior cul-de-sac, bilateral ovaries, and bilateral fallopian tubes could not be observed. The uterine defects were closed in a single layer with Vicryl 1-0 sutures. Subsequently, segmental resection of the small bowel and side-to-side anastomosis and adhesiolysis were performed.

Histopathological and immunohistochemical findings

The resected specimen consisted of an 11-cm-long segment of the terminal ileum (**Figure 1**), small bowel mesentery, placental disc, and umbilical cord. Grossly, the mesenteric surfaces were covered with gray white exudates and blood clots. The small bowel segment was markedly twisted because of inflammation and fibrous adhesion. Although the precise extent of the lesion was difficult to ascertain because of the severe distortion, it is thought to have been caused by inflammation due to intestinal content spillage as a result of mural tearing. The inflammatory reaction was limited to the mesenteric surface, and the serosa and subserosa of the small bowel. Well-defined placental tissue could not be observed with the naked eye. No neoplastic lesion was found, and the mucosal surface of the small bowel was unremarkable, except for a few areas of hyperemic and edematous changes. The placental disc and umbilical cord revealed no pathological abnormality.

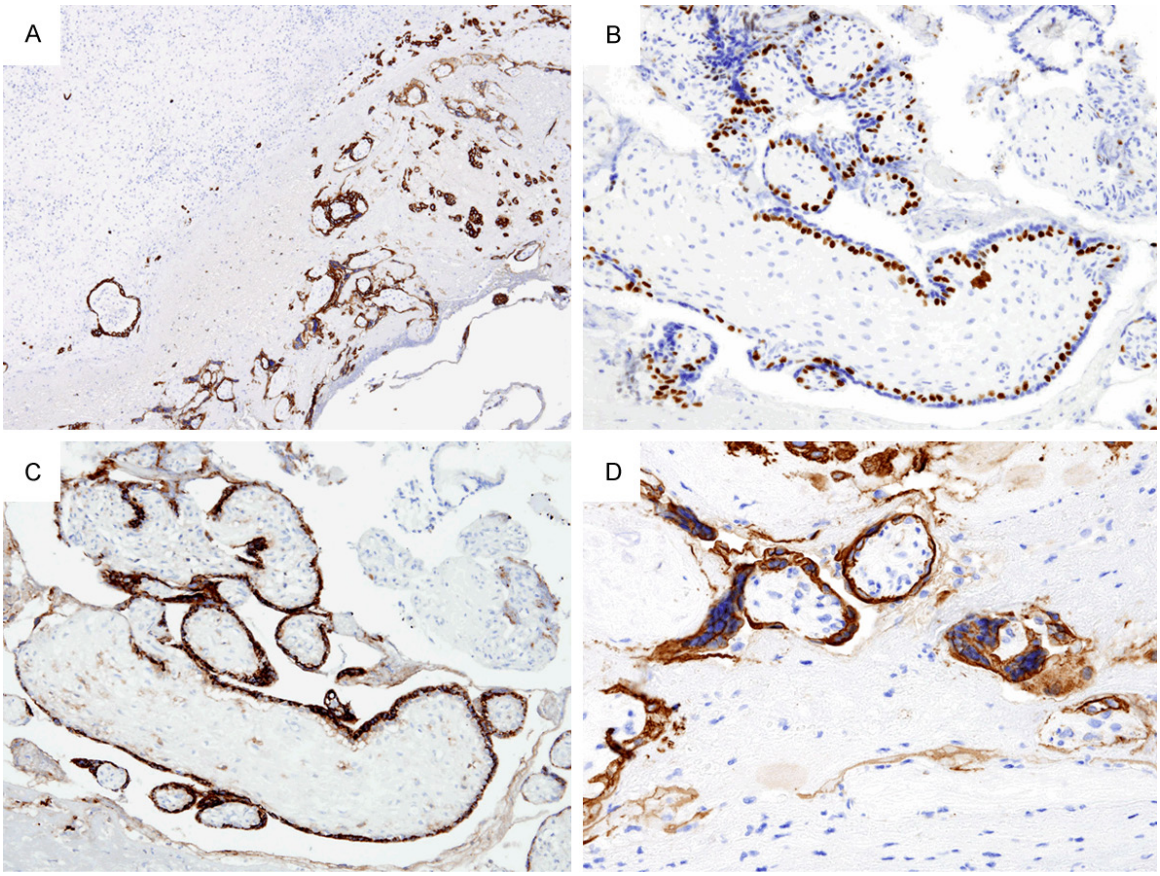

Figure 4. Immunohistochemical staining results. (A) The chorionic villi invading the subserosa exhibit cytokeratin expression. (B and C) The villous cytotrophoblasts demonstrate strong immunoreactivity to (B) p63 and (C) hCG. (D) hCG also highlights scattered syncytiotrophoblasts.

Microscopically, the serosa and subserosa of the terminal ileum and mesentery revealed acute purulent inflammation (**Figure 2A**). The inflammatory infiltrate extended obviously to the subserosa, but the mucosa, submucosa, and proper muscle were intact. The serosal surface was covered with fibrinous exudate admixed with scattered chorionic villi and syncytiotrophoblasts (**Figure 2B**). In some areas, extensive inflammatory response resulted in abscess formation (**Figure 2C**) and fibrinoid necrosis of the chorionic villi (**Figure 2D**). The chorionic villi appeared to attach to the serosal surface in most areas (**Figure 3A**), but occasionally, they seemed to invade the subserosal layer (**Figure 3B**). Irregularly shaped clusters of chorionic villi infiltrated the inflamed subserosa and were associated with hemorrhage and necrosis. In addition, the chorionic villi appeared to infiltrate superficially into the mesenteric fat (**Figure 3C**). The trophoblasts, villous stromal cells, and syncytiotrophoblasts did not show any cytological atypia (**Figure 3D**). No evidence of neoplastic lesion was identified. On immunohistochemical examination, the chorionic villi invading the subserosa were found to be uniformly positive for cytokeratin (**Figure 4A**). The villous cytotrophoblasts demonstrated strong nuclear p63 immunoreactivity (**Figure 4B**). Immunostaining for human chorionic gonadotropin also highlighted both the villous cytotrophoblasts (**Figure 4C**) and syncytiotrophoblasts (**Figure 4D**). Scattered trophoblasts were found, resembling intermediate trophoblasts and exhibiting immunoreactivity to both inhibin-α and p63. We considered that these findings reflect the data that the transition from cytotrophoblast to mature extravillous trophoblast involves a transitional trophoblast cell type that retains p63 and expresses inhibin [5].

Discussion

Placenta percreta is associated with maternal mortality as high as 10% and significant morbidity, mostly secondary to intraoperative hem-

orrhage and its consequences [6, 7]. Uterine rupture, a life-threatening complication, occurs in approximately 14% of patients with placenta percreta, before, during, or after labor [2, 8]. Placental invasion of adjacent organs (beyond uterine rupture) rarely occurs, but occurs mostly in the urinary bladder. Since the initial report by Ochshorn and colleague [9] in 1969, approximately 40 cases of placenta percreta invading the urinary bladder have been reported [10-17]. Case reports on placenta percreta with invasion of adjacent organs other than urinary bladder are rare. Among the causes of abnormally adhered placenta, the major pregnancy-related causes include histories of cesarean section and placenta previa. The fact that the anterior wall of the uterine corpus is opened during cesarean section and that placenta previa usually develops on the uterine anterior wall provide evidence supporting the possibility of placental tissue exposed to the abdominal cavity through the uterus invading the urinary bladder where it is adjacent to the uterine anterior wall.

In our patient, the placenta percreta involved the uterine anterior wall and fundus, and invaded the small bowel. The following are possible reasons why the abnormally adhered placenta showed widespread invasion of the small bowel, which is not normally involved. As gestational age increases, the uterus also increases in size, pressing on the urinary bladder inferiorly and reaching the level of the ribs superiorly. At full-term, because the uterine corpus can be located proximal to or can be in contact with the small bowel, colon, or abdominal organs, the adhesion and direct invasion of the adjacent bowel segment by placental tissue that penetrated the uterus would have been difficult to detect by using antenatal ultrasonography. In fact, because of the associated high morbidity and mortality in placenta percreta, many researchers have developed methods for early and accurate diagnosis of placenta percreta by using antenatal ultrasonography. As a result, several imaging findings have been presented that suggest the possibility of an invasive placenta located on the previous uterine scar area, including the following: an absence of thinning (less than 1 mm) of the normal hypoechoic myometrial zone; the presence of lacunar vascular spaces or lakes; irregularity or disruption of the hyperechoic bladder-uterine interface; extension of placental tissue beyond the uterine serosa; and the presence of increased vasculature (highlighted by color Doppler ultrasonography) on the surface of the uterus [18-20]. Nevertheless, in spite of such research results and improvements in radiology, most cases of abnormally adhered placenta are not diagnosed prenatally and are discovered at the time of delivery [21]. It is suggested that more-detailed ultrasonographic tests and follow-up studies are required for such cases.

Painless third-trimester prepartum hemorrhage can be associated with placenta previa. By contrast, vaginal bleeding caused by placenta percreta is more likely to be painful because of invasion of the bleeding placental tissue into the uterine wall. Although some patients with placenta percreta have been reported to experience a dull, continuous lower abdominal pain during their pregnancy [10], most patients with placenta percreta do not have any symptoms. In this case, histopathologically acute suppurative and gangrenous inflammation was observed not only in the small bowel subserosa and mesentery involved with the placental tissue but also in the surrounding serosa. This observation strongly suggests the possibility of prenatal uterine rupture caused by invasive placental tissue and microperforation due to direct extension to the small bowel. In addition, the severe fibrous adhesion between the abdominal organs observed at the time of delivery suggests that these inflammatory reactions such as peritonitis had persisted for a long time. According to previous research results, placenta percreta is difficult to diagnose in some cases where it does not cause specific symptoms or signs, and even if symptoms do develop, they are not significantly different from conditions that can be caused by normal pregnancy such as abdominal discomfort, lower abdominal pain, vaginal bleeding, and hematuria [10]. During follow-up monitoring of pregnant women with predisposing factors for abnormal placental adherence, careful history taking by the clinician and the use of detailed ultrasonographic tests are important for early diagnosis and proper treatment.

In summary, the aim of this report is to describe a neglected case of placenta percreta that was initially managed conservatively in a patient who developed intraoperative uterine rupture, intra-abdominal hemorrhage, and small bowel perforation. The patient had a history of cesar-

ean section for placental abruption. Placenta percreta is associated with high maternal mortality and morbidity rates, mostly secondary to intraoperative hemorrhage and its consequences. A high index of suspicion for placenta percreta is required when evaluating pregnant women with a history of cesarean delivery. Imaging studies may be useful in establishing the diagnosis preoperatively. The risks of fetal and maternal morbidity and mortality rates may be reduced through proper planning and a multidisciplinary approach.

Acknowledgements

This study was supported by a faculty research grant of Yonsei University College of Medicine for 2016 (6-2016-0130).

Disclosure of conflict of interest

None.

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References

[1] Clement PB, Young RH. Atlas of Gynecologic Surgical Pathology. Philadelphia, PA: Saunders Elsevier; 2014.

[2] Fox H, Sebire N. Pathology of the Placenta. Philadelphia, PA: Saunders Elsevier; 2007.

[3] Miller DA, Chollet JA, Goodwin TM. Clinical risk factors for placenta previa-placenta accreta. Am J Obstet Gynecol 1997; 177: 210-214.

[4] Wu S, Kocherginsky M, Hibbard JU. Abnormal placentation: twenty-year analysis. Am J Obstet Gynecol 2005; 192: 1458-1461.

[5] Kaspar HG, Crum CP. The utility of immunohistochemistry in the differential diagnosis of gynecologic disorders. Arch Pathol Lab Med 2015; 139: 39-54.

[6] Hudon L, Belfort MA, Broome DR. Diagnosis and management of placenta percreta: a review. Obstet Gynecol Surv 1998; 53: 509-517.

[7] Price FV, Resnik E, Heller KA, Christopherson WA. Placenta previa percreta involving the urinary bladder: a report of two cases and review of the literature. Obstet Gynecol 1991; 78: 508-511.

[8] Esmans A, Gerris J, Corthout E, Verdonk P, Declercq S. Placenta percreta causing rupture of an unscarred uterus at the end of the first trimester of pregnancy: case report. Hum Reprod 2004; 19: 2401-2403.

[9] Ochshorn A, David MP, Soferman N. Placenta previa accreta. A report of 9 cases. Obstet Gynecol 1969; 33: 677-679.

[10] Abbas F, Talati J, Wasti S, Akram S, Ghaffar S, Qureshi R. Placenta percreta with bladder invasion as a cause of life threatening hemorrhage. J Urol 2000; 164: 1270-1274.

[11] Caliskan E, Tan O, Kurtaran V, Dilbaz B, Haberal A. Placenta previa percreta with urinary bladder and ureter invasion. Arch Gynecol Obstet 2003; 268: 343-344.

[12] Essatara Y, Benazzouz H. Placenta percreta with bladder invasion. Pan Afr Med J 2014; 18: 88.

[13] Parva M, Chamchad D, Keegan J, Gerson A, Horrow J. Placenta percreta with invasion of the bladder wall: management with a multidisciplinary approach. J Clin Anesth 2010; 22: 209-212.

[14] Shawish FM, Hammad FT, Kazim EM. Placenta percreta with bladder invasion. A plea for multidisciplinary approach. Saudi Med J 2007; 28: 139-141.

[15] Sijanovic S, Rubin M, Topolovec Z, Vidosavljevic D, Sijanovic I. Placenta previa percreta with bladder invasion. Med Glas (Zenica) 2011; 8: 66-68.

[16] Takai N, Eto M, Sato F, Mimata H, Miyakawa I. Placenta percreta invading the urinary bladder. Arch Gynecol Obstet 2005; 271: 274-275.

[17] Yanagisawa T, Furuta A, Egawa S, Tanaka T. [A case report of placenta percreta with bladder invasion]. Hinyokika Kiyo 2012; 58: 283-286.

[18] Chen CH, Wang PH, Lin JY, Chiu YH, Wu HM, Liu WM. Uterine rupture secondary to placenta percreta in a near-term pregnant woman with a history of hysterotomy. J Obstet Gynaecol Res 2011; 37: 71-74.

[19] Sumigama S, Itakura A, Ota T, Okada M, Kotani T, Hayakawa H, Yoshida K, Ishikawa K, Hayashi K, Kurauchi O, Yamada S, Nakamura H, Matsusawa K, Sakakibara K, Ito M, Kawai M, Kikkawa F. Placenta previa increta/percreta in Japan: a retrospective study of ultrasound findings, management and clinical course. J Obstet Gynaecol Res 2007; 33: 606-611.

[20] Teo SB, Kanagalingam D, Tan HK, Tan LK. Massive postpartum haemorrhage after uterus-conserving surgery in placenta percreta: the danger of the partial placenta percreta. BJOG 2008; 115: 789-792.

[21] Chou MM, Chen WC, Tseng JJ, Chen YF, Yeh TT, Ho ES. Prenatal detection of bladder wall involvement in invasive placentation with sequential two-dimensional and adjunctive three-dimensional ultrasonography. Taiwan J Obstet Gynecol 2009; 48: 38-45.