



CHORIONIC VILLI IN THE CHRONIC ENDOMETRITIS.

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SUMMARY

Objective: The aim of this study was to examine the structure of the placental villi in the chronic endometritis at 8 weeks of pregnancy without another antecedent of illness and evaluated with light microscopy.

Study design: Placenta study and placenta normal were compared. Placenta study proceeds of patient of 28 years old with problems of infertility and medical history of recurrent abortion and dysfunctional uterine bleeding.

Results: The decidual region showed an infiltration of leucocytes polymorphonuclears with plasma cells. The villi showed anaplastic feature, increased growth and multiplication of citotrophoblast cells associate with giant multinuclear cells, intervillous thrombosis, immaturity, debris of tissue death and degenerated villi associate to endometrium in degeneration.

Conclusion: These results indicate the vulnerability of the trophoblast during infection increasing the mechanisms that produce the abortion.

KEY WORDS: Chorionic villi endometritis abortion

INTRODUCTION:

Endometritis is an infectious and inflammatory disorder of the endometrium. Chronic endometritis (CE) is characterized by endometrial superficial edematous change, high stromal cell density; dissociated maturation between epithelium and stroma, and infiltration of endometrial stromal plasmocytes cells (ESPCs)¹. The presence of multiple ESPCs is the most frequent findings in this pathology². This long-neglected gynecologic disease, with subtle symptoms as pelvic discomfort, spotting, leucorrhea, often unnoticed by patients, being a benign disease, not has been described as associated with placental villi and histopathologic examinations appear not to be favored by gynecologic practice³.

The microorganisms in endometrium with chronic endometritis are: Streptococcus species, Escherichia coli, Enterococcus faecalis, Staphylococcus species, Mycoplasma/Ureaplasma species: Mycoplasma genitalium, Mycoplasma hominis, and Ureaplasma urealyticum, Proteus species, Klebsiella pneumonia, Pseudomonas aeruginosa, Gardnerella vaginalis, Chlamydia trachomatis, Neisseria gonorrhoeae, Corynebacterium and yeasts: Saccharomyces cerevisiae and candida species⁴. Mycobacterium tuberculosis has been mentioned as a microorganism causing a poorly developed caseating granuloma and surrounding lymphocyte infiltrates including ESPCs⁵. Altered proportions in anaerobic lactobacilli species, human immunodeficiency virus and cytomegalovirus also have been reported in CE. The histopathologic detection of multiple ESPCs in endometrial biopsy is of primary importance in the diagnosis of CE in current clinical practice³.

Plasmacytes typically have a large cell body, high nuclei/cytoplasm ratio, basophilic cytoplasm and nuclei with heterochromatin rearrangement as the "spoke wheel"⁶. The identification of glandular-stromal dyssynchrony and endometrial eosinophil infiltrates (cytoplasmic eosinophilic granules) on routine hematoxylin and eosin staining sections was proposed as a convenient screening tool to discover ESPCs but are not the absolute findings in CE⁷.

Histopathologic evaluation using immunohistochemistry for plasmacyte marker CD138 (Known as syndecan-1, a transmembrane type heparin sulfate proteoglycan) is currently the most reliable and time saving diagnostic method for CE⁸.

Stringent criteria have not yet been established for the evaluation of the ESPCs density in the endometrial biopsy specimen although the presence of multiple (two or more) ESPCs is a sine qua non for the confirmation of CE. There are some biases and variances in definitions of CE among the studies. While one study diagnosed CE with more of five CD138(+)ESPCs in at least one out of three sections levels in the endometrial biopsy specimens, others set the values for CE as one or more CD138(+)ESPCs in one macroscopic high-power field⁹.

Maternal infections caused by the microorganisms mentioned which can cross the placenta, may result in abortion or stillbirth. Pathogens can reach the deciduas only by dissemination in maternal cells, most likely leukocytes. If the defense mechanisms of the extravillous trophoblast are overcome, the infection may spread to the fetal blood, act as a nichus for maternal reinfection, and or cause trophoblastic death resulting in placental insufficiency or spontaneous abortion. Some pathogens may reach the fetus by traveling within maternal leukocytes on their natural way to the fetus¹⁰. The visualization of the placental villi and their interactions with the endometrium in this hostile ambient not have been observed and require to be investigated.

The aim of this study was to describe the histomorphology of the placental villi during this inflammatory process associated to endometritis.

MATERIAL AND METHODS:

Patient of 28 years old who refers in her medical history intrauterine death to 8 weeks of gestation and abortion, with clinical antecedents of pelvic discomfort, spotting, leucorrhea, with anterior abortion, problems of infertility, dysfunctional uterine bleeding and

endometrial sampling for histological investigation. Diagnosed with endometritis to the six weeks of the gestation. The infected woman pregnancy had knowledge of informed consent and approval by the ethical committee of the hospitalary institution for the realization of this investigation according to the Helsinki Declaration. One specimen of endometrial biopsy was taken in the hospitalary institution and sent to us for their microscopic study. No microbiologic investigation of the material was realized. Ten slides microscopic were prepared and stained with H&E for their observation. Histological diagnosis of chronic endometritis was based on the criteria previously described¹¹, stromal edema, and hyperhemia. Chronic endometritis was defined as the presence of plasma cells in the endometrial stroma, including superficial stromal edema, increased stromal density, spindled stroma and polymorphic inflammatory cells^{1, 12}.

RESULTS:

Observations realized in the deciduas permitted to identify an infiltration of leukocytes polymorphonuclears which indicates an infectious and inflammatory disorder (Fig.1).

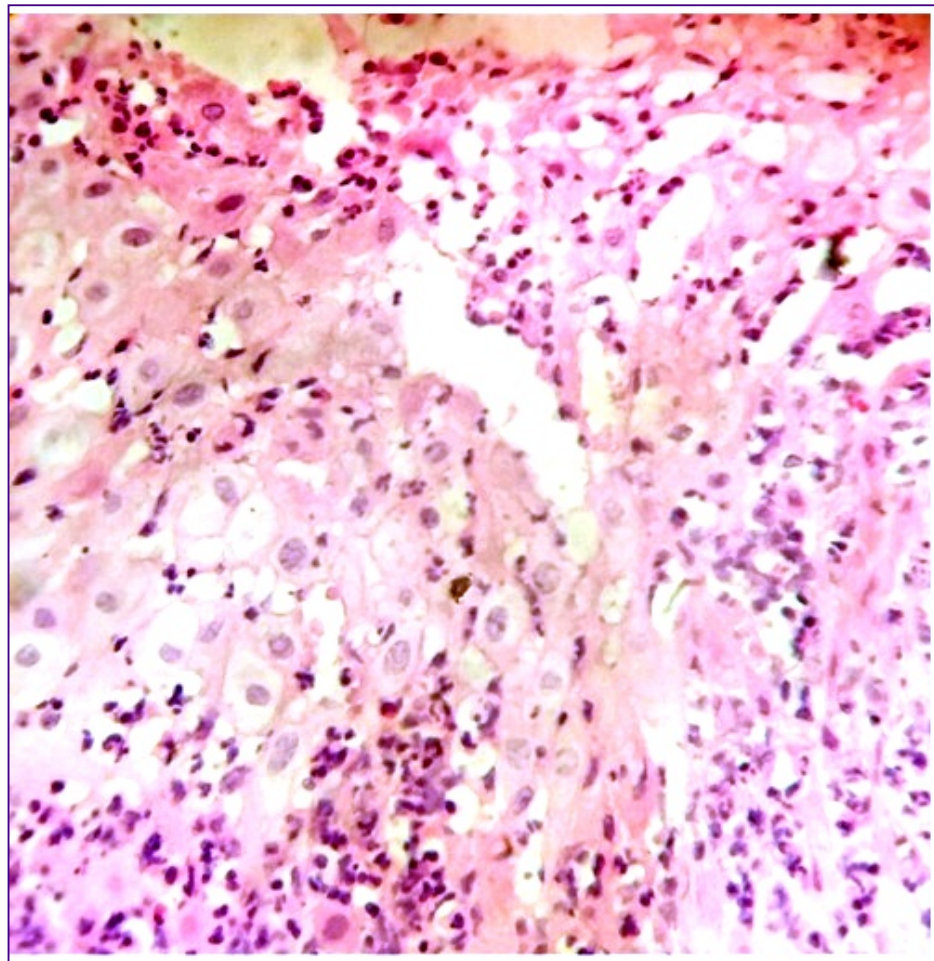


Fig.1. A severe deciduitis is observed in the microphotography. H&E.400x

In this numerous poblation of leukocytes, plasma cells and eosinophil leukocytes were observed (Fig2).

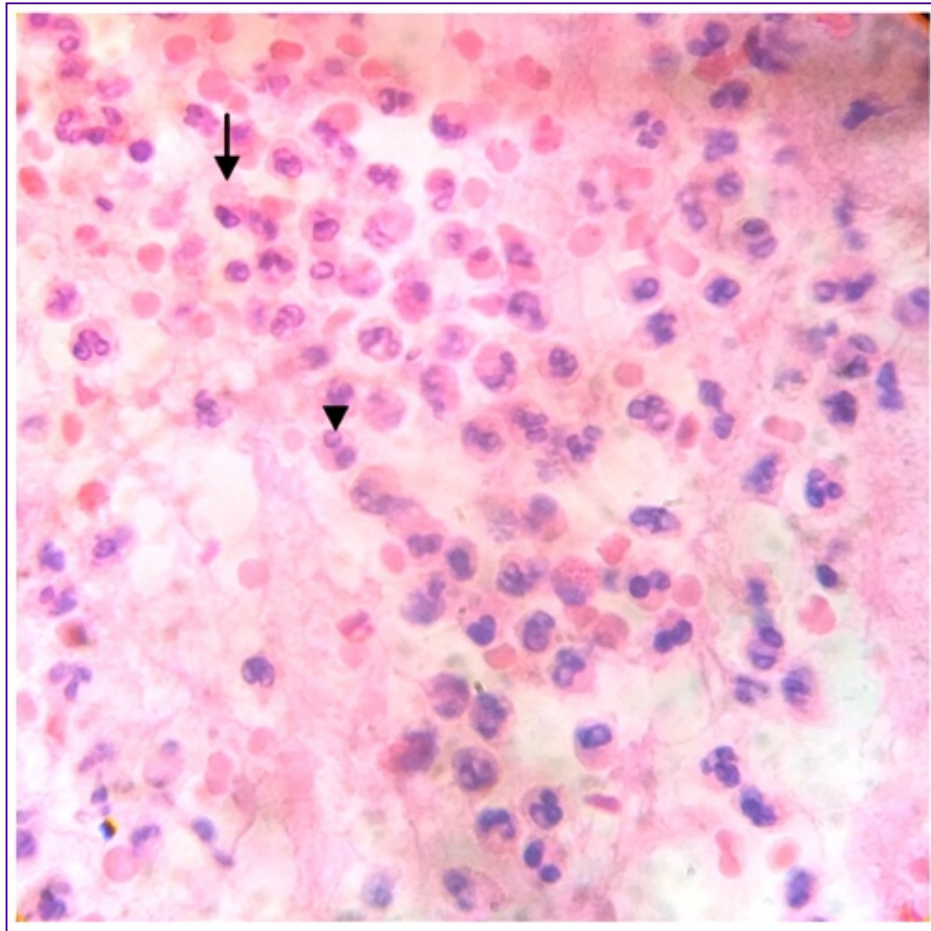


Fig.2. Plasma cells (arrow) and Eosinophil leucocytes (head of arrow) are seen in this section of degenerated tissue. H&E.400x

In some regions of the endometrium the placental villi appeared showing their anaplastic feature at level of the trophoblast (Fig.3).

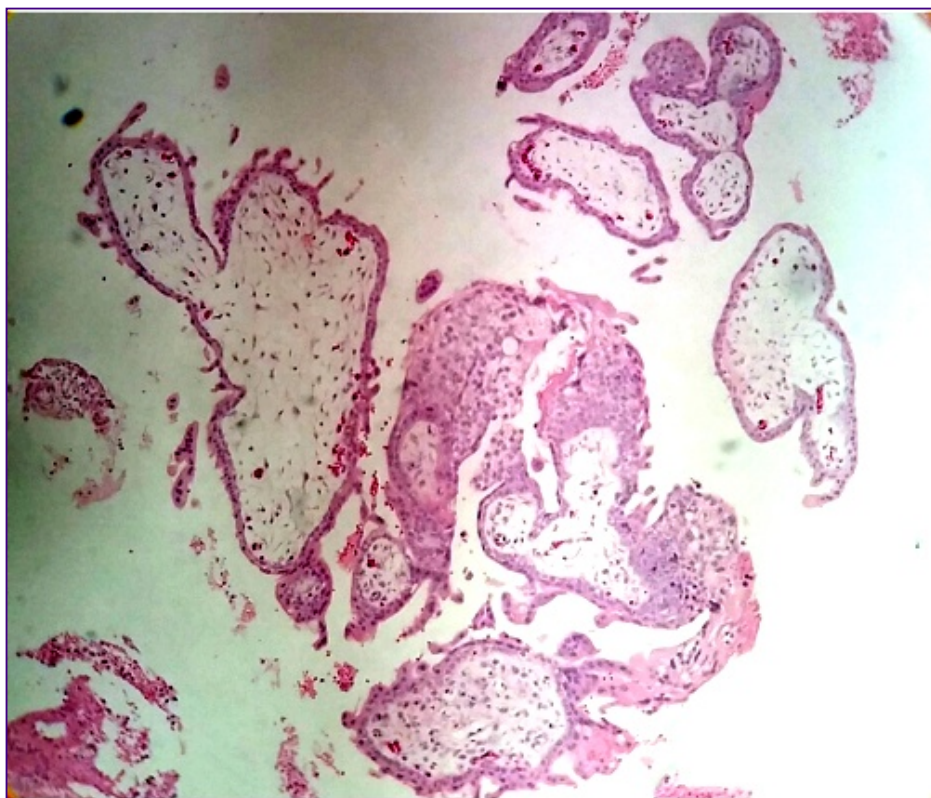


Fig.3. The trophoblast in these sections of villi shows their anaplastic feature. H&E.100x

An increased growth and multiplication of citotrophoblast cell associate with giant

multinuclear cells was observed in the endometrial biopsy (Fig.4).

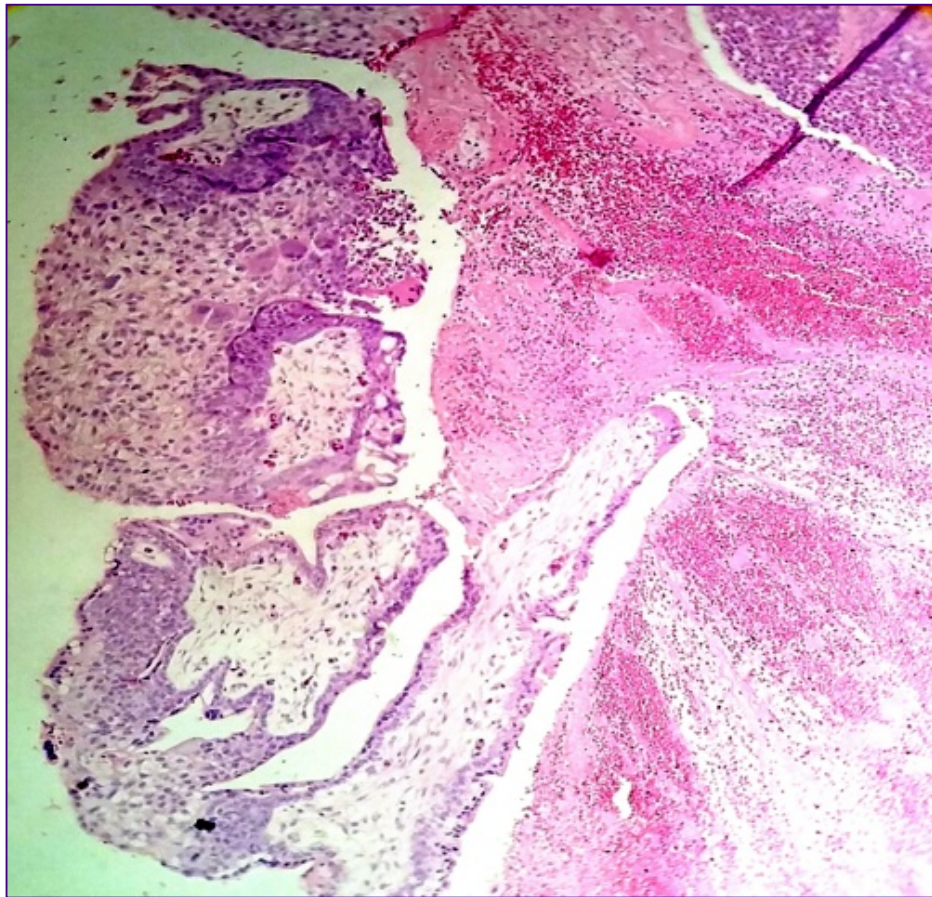


Fig.4. The trophoblast is seen increased and separating of the infected endometrium. H&E.100x

Thrombosis intervillous can to be noted in some regions of the endometrium (Fig.5).

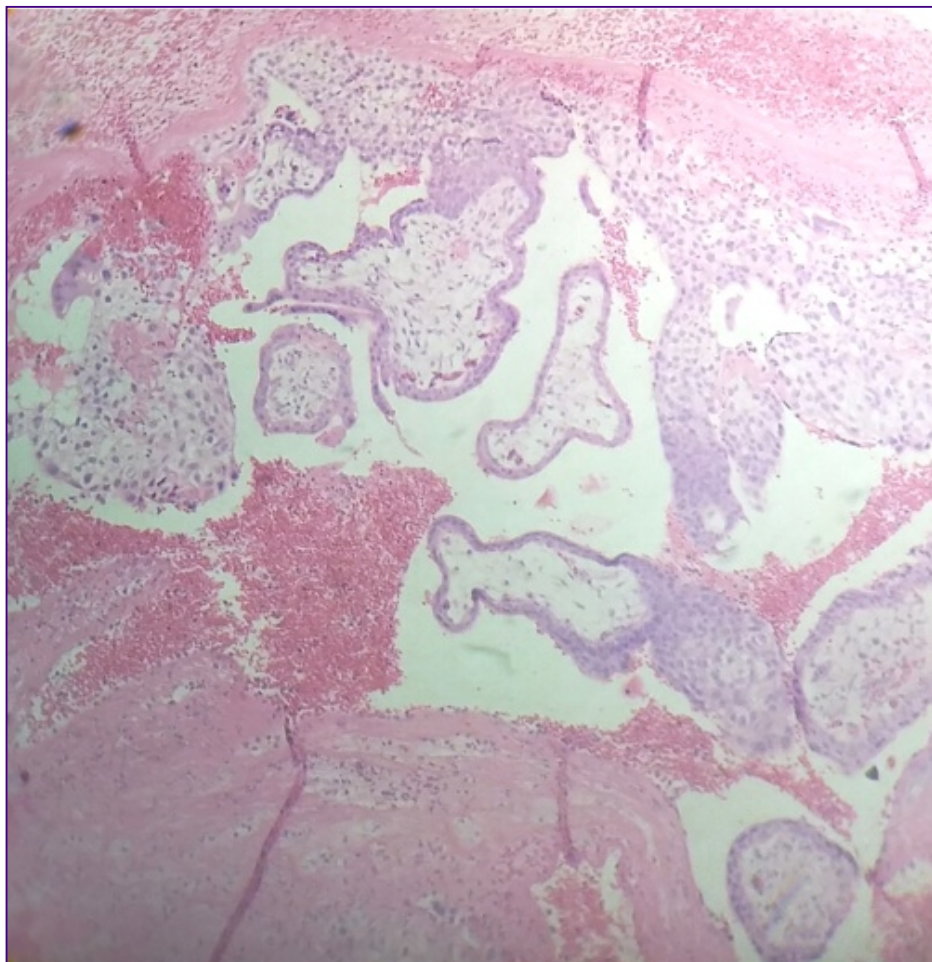




Fig.5. Intervillous thrombosis is surrounding to degenerated trophoblast. H&E.100x

Some villi shows their immaturity with stromal vessels that contain nucleated erythrocytes (Fig.6).

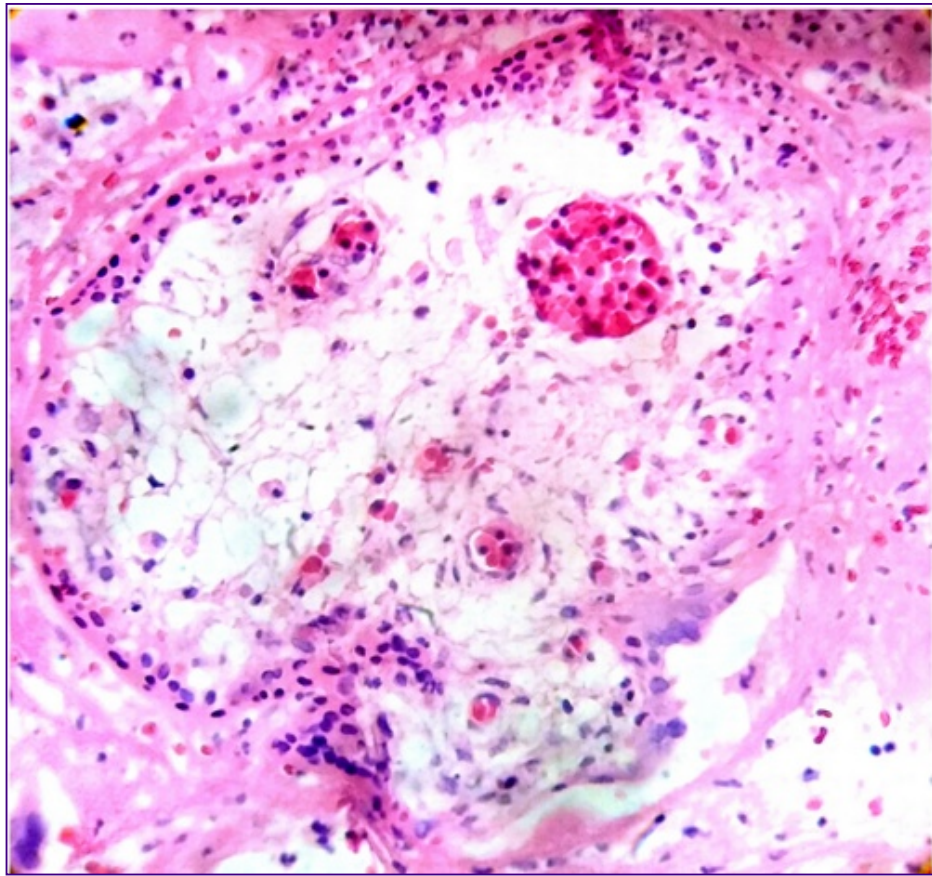


Fig.6. Nucleated erythrocytes in stromal vessels of an immature villi. H&E.400x

In the endometrial tissue debris of tissue death were observed (Fig.7).

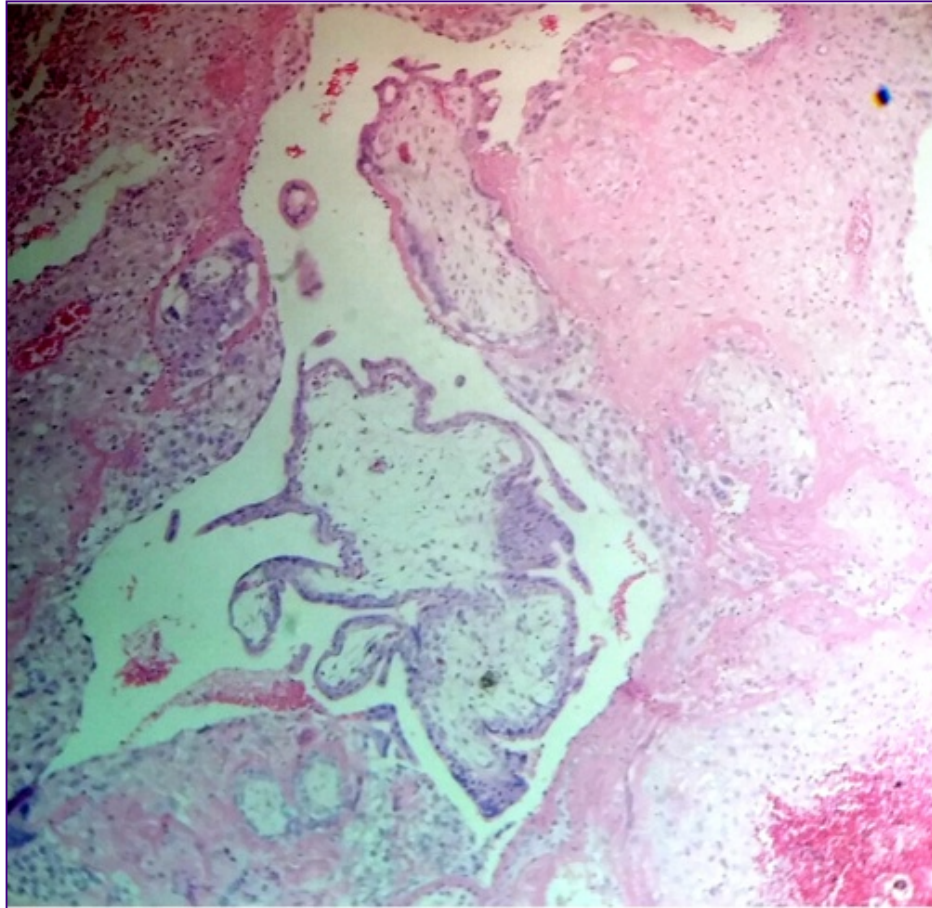


Fig.7. A villi is connected still to endometrium. H&E.100x

Chorionic villi is observed in connexion with an inflamed endometrium and in other regions they are as separating (Figs.8,9).

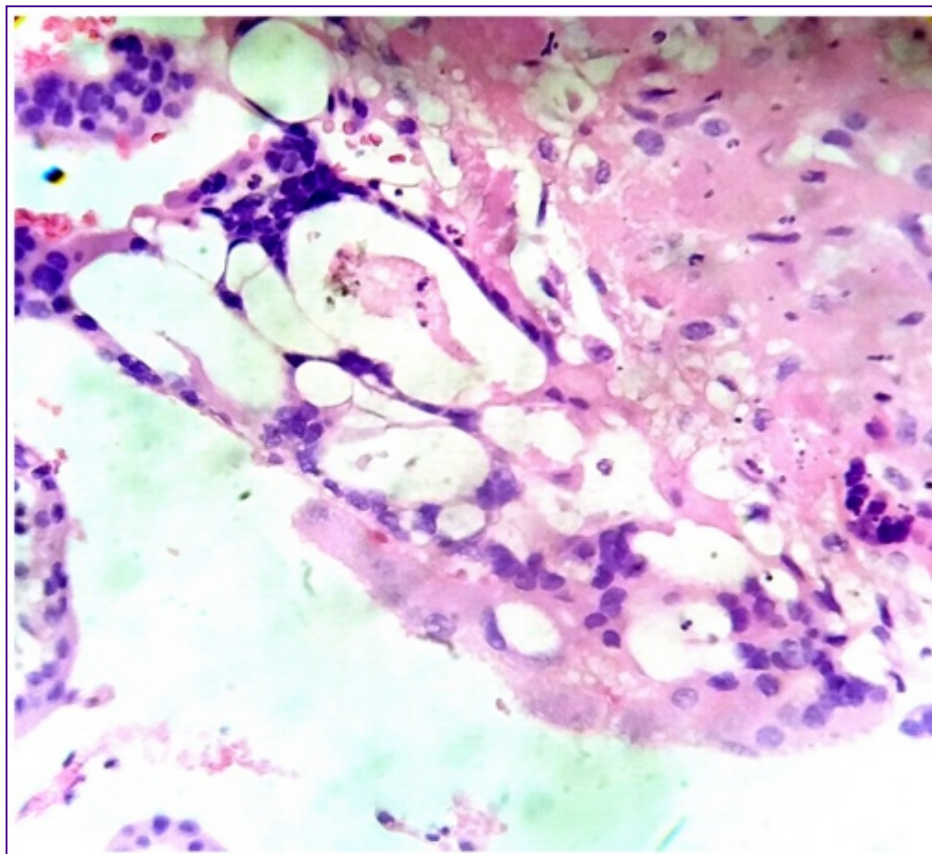


Fig.8. Both structures, placental villi and endometrium, are suffering a degenerative process. H&E.400x

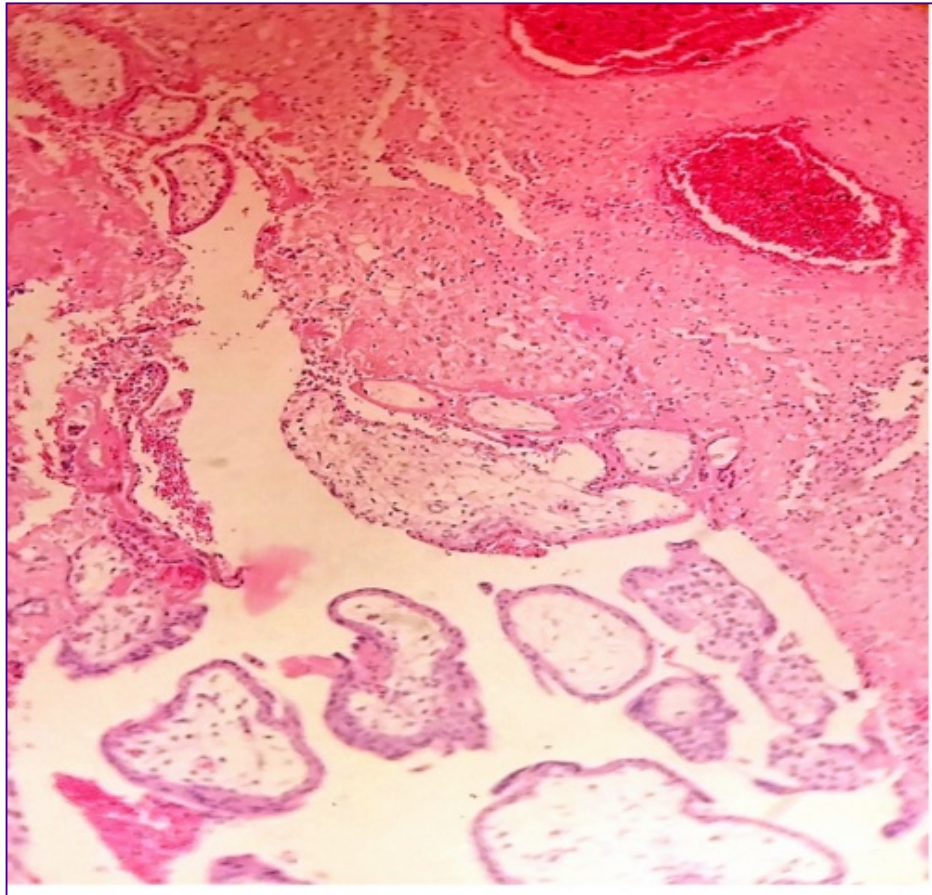


Fig.9. The villi which penetrated the endometrium have degenerated in their interior and has tendency to be separated.
H&E.100x

Degenerated villi are seen associated to the endometrium which also suffers a process of degeneration (Fig.10).

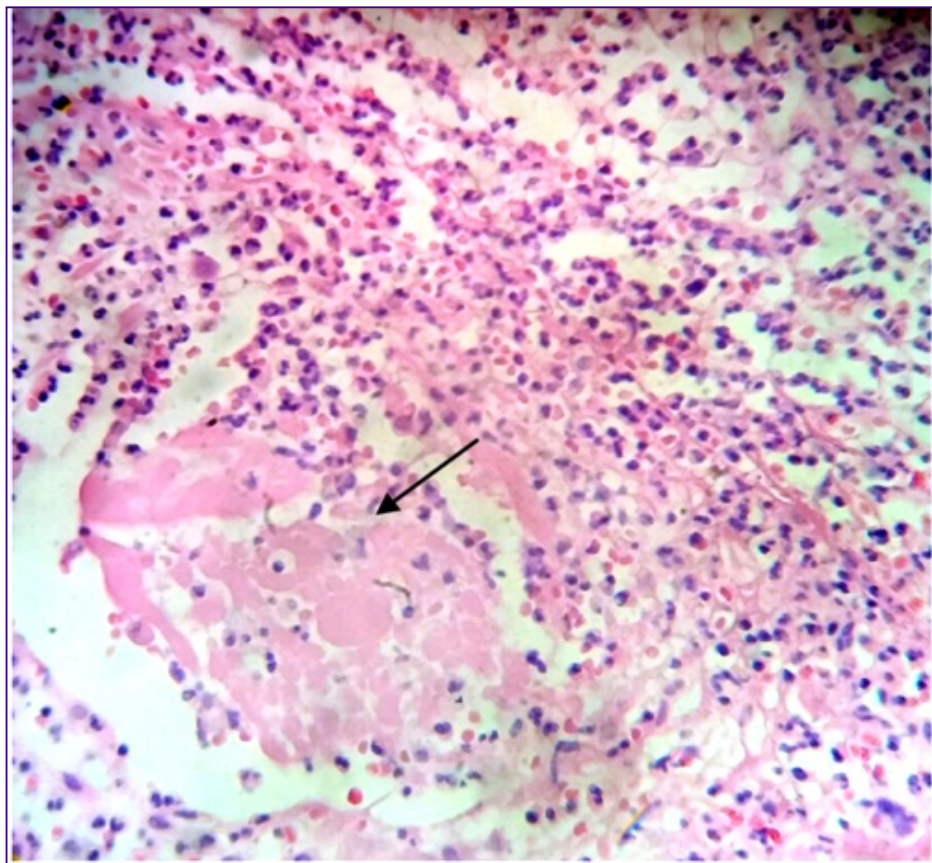


Fig.10. Debris of tissue death can be noted (arrow). H&E.100x

DISCUSIÓN

The microorganisms of the Group B *streptococci*, *Escherichia coli*, *Corynebacterium*, *Gardnerella vaginalis*, *Ureaplasma urealyticum*, *Mycoplasma* and *Staphylococcus* may cause chorioamnionitis during pregnancy and provoke repeated abortion. In our case an acute and chronic deciduitis in an immature placenta with chorioamnionitis inflamed the region where the placenta was inserted and the posterior necrosis of the zone makes a premature rupture¹³.

The identification of plasma cells and eosinophils cells in endometrial tissue could to be seen with light microscopy in this material obtained of abortion and the presence of polymorphonuclear leukocytes (PMNLs) was also observed in the villi.

The ascendant infection inflamed the membranes and the amniotic cells synthesized prostaglandins that increased the delivery and the PMNLs secreted elastases and collagenases that initiated the premature rupture^{14, 15}.

In their anaplastic feature the prolongations of the trophoblast intended to penetrate the endometrium and sections of villi were seen associate to the stromal region where suffered degenerative changes. This proliferative extent of trophoblast has been examined in specimens from spontaneous abortions that were seen in trisomy 7 and 15¹⁶. The diminished blood flow into the intervillous space at an early gestational age can to produce thrombosis intervillous which is of importance in causing spontaneous abortion¹³.

The observation of nucleated erythrocytes in these immature intermediate villi indicates a permanent blood circulation¹⁷.

Thrombophilia and a maternal immunological mechanism whose antibodies probably could to provoke the lysis of decidual cells in our case and of this mode to originate a severe premature placental detachment of normal insert placenta or a severe placental abruption. It is possible that antiphospholipid antibodies as immunoglobulins IgG, IgM, IgA which appear in bacterial and viral infections provoked the death of decidual and trophoblast cells damaging the structural organization of their cell membranes¹⁸

Placental villi which gets connects to the endometrium suffers furtherly a process of degeneration and finishes in this hostile ambient with detachment of the extracellular fibrinoid matrix in the thickness of the basal plate.

It seems that in chronic endometritis the placental villi acquires a neoplastic feature own of tumours. Masses of trophoblast have been seen invading the myometrium and disrupting its architecture, undergoing degeneration, nuclear pleomorphism and simulating a sarcoma. They can to invade blood vessels and to be present within lumen being confused as choriocarcinoma. Notwithstanding, trophoblast has ability to invade without assuming character of malignant tumor and this exaggerated expression of invasion as trophoblastic pseudotumor simulates a malignant tumor¹⁹.

The literature indicates that an embryochorionic insufficiency provoked by local inflammation as endometritis and insufficient cytotrophoblast invasion with secondary changes in placental villi could give rise to an early spontaneous abortion²⁰.

In material of curettings biopsies the immunoperoxidase localization of human placental lactogen has been used as marker for the placental origin of the giant cells in "syncytial endometritis" of pregnancy²¹.

An epidemiologic study supports the idea that chronic deciduitis originates in preconceptional chronic endometritis rather than in ascending infection during the gestational period²². In this study, the exploration of data set developed in placentas between 22 and 32 weeks from non anomalous singleton liveborn infants; the histopathologic lesions showed in women with recurrent preterm delivery were: amnionitis, chorionitis, deciduitis, vasculitis, vessel fibrinoid necrosis, atherosclerosis, decidual hemosiderin, histological features of placental abruption, cytotrophoblast proliferation, nucleated erythrocytes, thrombosis intervillous, fibrin deposition, villous infarction, fibrosis, hypovascularity, stromal mineralization, hemorrhagic endovasculitis, decidual eosinophilia, plasma cell in basal plate and villitis of anchoring villi²².

So, endometritis perturbs the transformation of stromal cells to decidual cells provoking in the decidualization an unstable adaptation of the trophoblast cells in the decidua during the gestation which increases the mechanisms that produces the abortion. The trophoblast not obtains good implantation and terminates degenerating in contact with the endometrium²³.

No chronic villitis was seen in our case, since very few lymphocytes were noted infiltrated in the placental villi with absence of plasma cells and histiocytes²⁴.

Syncytiotrophoblast resist infection; however, the immature cytotrophoblast of cell columns, most prominent in this trimester, is more vulnerable to infection increasing the possibility of abortion. Many cases of chronic villitis lacking a clinical history of infection or characteristic viral cytopathic effects are attributed to a maternal alloimmune response to trophoblast antigens²⁵.

Aside from the lack of detectable placental organisms, absence of maternal or neonatal signs, symptoms, and the absence of treatment in CE, the presence of intervillitis and neutrophils should raise the suspicion for infection and consideration of histologic special stains for the detection of villitis²⁶.

The most common findings in early abortions, under 12 weeks, were hydatid degeneration cystic, severely edematous, with atrophic trophoblast and without evidence of trophoblastic hyperplasia²⁷. However, in our case scanty lymphocytic villitis without hydatid degeneration could indicate the no envelopment of chromosomal anomaly. In these cases of endometritis also has been found hypermaturity and/or villous immaturity as main histological patterns²⁸.

This illness has been reviewed recently as the second cause of maternal death in the post partum²⁹. Patients suffering from chronic endometritis may have an underlying cancer of the cervix or endometrium and to be associated with cervical hypertrophy and induction of squamous metaplasia contributing in the development of cervical neoplasia among women with persistent high risk HPV infection³⁰. By other hand, altered uterine contractility in these patients could lead to uterine dysperistalsis as cause that impeded the normal association of the placental villi to the endometrium as seen in fig.4²³.

In conclusion, during the endometritis an utero infected no permit the normal implantation of the villi by damage to the trophoblast which suffers degenerative changes for aggregating to the endometrium and increasing the mechanisms that provoke the abortion.

CONFLICT OF INTEREST: The author reports no conflict of interest.

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