

Blighted ovum: ultrasonic, histopathologic and hormonal considerations

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Summary: Thirty women experiencing early pregnancy failure (blighted ovum) were studied at frequent intervals with serial measurements of serum human chorionic gonadotropin (β -hCG), progesterone (P_4) and estradiol (E_2). The diagnosis of blighted ovum had previously been made by careful ultrasonic examination (s). Histopathologic findings in the placenta were studied in all cases. Hormonal levels were variable and in most of the cases indistinguishable from normal pregnancies. In only 50% of the cases the histopathologic examination revealed findings compatible for the blighted ovum criteria.

Key words: Blighted ovum; Diagnosis; Pathology.

INTRODUCTION

The term blighted ovum has been used to describe an impregnated ovum whose development has become arrested at an early gestational stage before completion of the first trimester, whereas the histopathologic examination of the abortive tissues does not reveal any recognisable fetal part. It is estimated that the incidence of blighted ovum is 49% to 90% in spontaneous abortions overall, and chromosomal abnormalities are present in 50% of such cases (^{1, 2}).

For the diagnosis of this common cause of early pregnancy failure emphasis was placed in the radioimmunologic estimation of human chorionic gonadotropin (hCG), pregnancy specific β_1 -glycoprotein, human

placental lactogen (hPL), progesterone (P_4) and estradiol (E_2) in maternal plasma with varied prognostic value (³⁻⁵). Sonography was also extensively used and in experienced hands seems to offer reliable differentiation of blighted and normal ova from eight to ten weeks of gestation (⁶⁻⁸).

The present study was undertaken to evaluate the endocrine profile in patients with blighted ovum, taking into consideration the histopathologic characteristics of the abortive tissues.

MATERIALS AND METHODS

The material consisted of 30 pregnant women (mean age 28 ± 4.4 years) who were admitted to the Department of Obstetrics and Gynecology because of uterine spotting or bleeding and miscarried between the 9th and 14th weeks of gestation.

The ultrasonic diagnosis of blighted ovum was made in all cases after 2 or 3 examinations had been performed. The equipment used was picker 5000 real time linear array ultrasonic scanner. The main ultrasonic marker was an empty but clearly defined gestational sac in the

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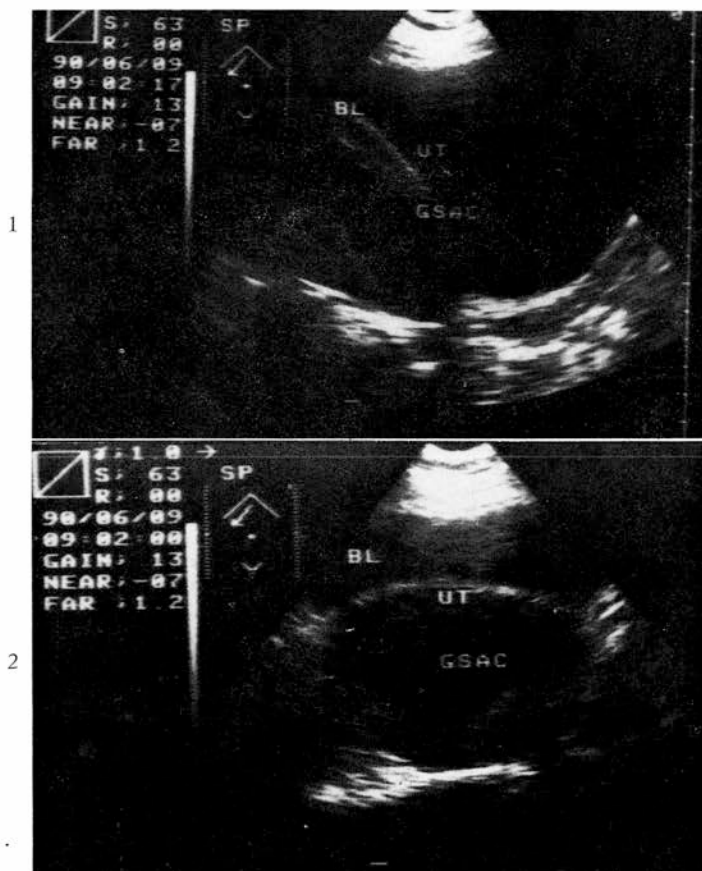


Fig. 1. — Longitudinal ultrasonic section of the empty gestational sac (GS) in the uterus (10th week of amenorrhea).

Fig. 2. — Sagittal ultrasonic section of the empty gestational sac (GS) in the uterus (the same case).

uterus (Fig. 1, 2). Repeated examinations showed a lack of fetal echoes and lack of an increase in diameter of the gestational sac compatible with gestational age. Peripheral venous blood samples were randomly obtained for estimation of β -subunit human chorionic gonadotropin (β -hCG), estradiol (E_2) and progesterone (P_4) levels.

The outcome of pregnancy was spontaneous abortion in 22 cases (mean gestational age 7 weeks), whereas in 8 cases with gestational age between 10-14 weeks evacuation of the uterus was electively performed on the basis of the ultrasonic findings. The specimens were sent to the pathology department for histopathologic examination.

The main histopathologic criteria used for the diagnosis of blighted ovum were absent or defective vascularity, hydropic degeneration of the stroma, large villi and great variation in the size of villi or villous hypoplasia with small and poorly vascularized villi and a hypoplastic trophoblast (Figure 3) (9). The histopathologic evaluation was made in all these patients at the 9th to 14th week of gestation.

RESULTS

Of the 30 cases with the diagnosis of blighted ovum made by ultrasonic methods in the histopathologic examination of the

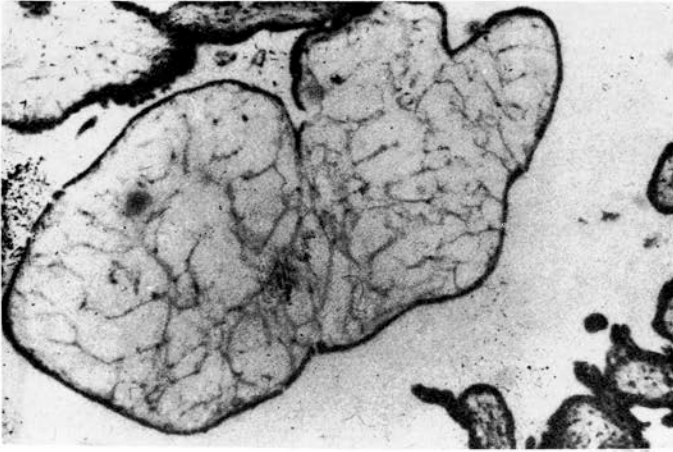


Fig. 3. — Blighted ovum. Great variation in the size of the villi and hydropic degeneration of the stroma of the large villous (center, H-E $\times 250$).

abortive tissue the villi and stroma were ascertained as normal in 10 cases (33%). In 15 cases (50%) the histopathologic findings of the villi and stroma fulfilled the compatible criteria for blighted ovum criteria (Fig. 4) whereas in 5 cases (16.7%) the diagnosis of possible blighted ova was made (Fig. 5) and that because of the post-mortem abortive tissue changes making the primary pathologic futures of villi and stroma uncertain.

The hormonal values of serum β -hCG, E_2 and P_4 of the 30 patients are shown in Figures 6-8. The hatched area represents the 95% tolerance limits of the normal population (127 women with normal term singleton pregnancies).

Eight (26.7%) patients had low but normal β -hCG values at the beginning of pregnancy (5th - 6th week) decreasing afterwards into lower than the normal levels. All other patients had β -hCG le-



Fig. 4. — Blighted ovum. Hydropic degeneration and poor vascularity of the villous stroma (H-E $\times 250$).

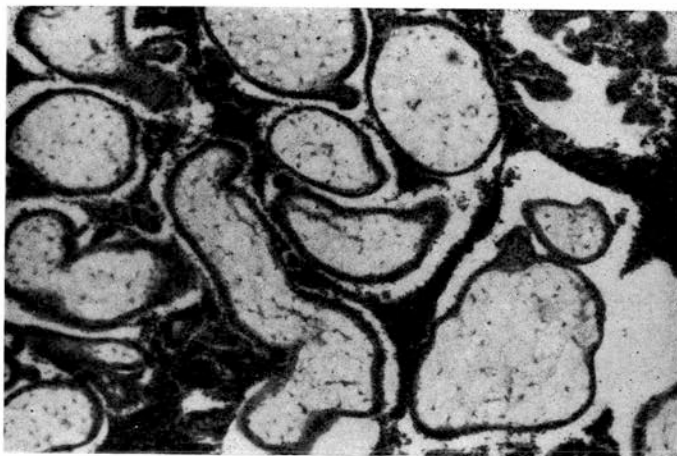


Fig. 5. — Possibly blighted ovum. Medium sized villi with hydropic stroma but without variation in size (H-E $\times 250$).

vels lower than normal throughout their gestations (Fig. 6).

Plasma progesterone values were also variable. Twelve (40%) patients had values within or above the 95% confidence limits with a clear decrease noted between 7th to 8th week. All other patients had serum progesterone levels below the normal range (Fig. 7).

Fourteen (46.7%) patients had estrogen values within the normal range at the 6th and 8th weeks but clearly decreasing from the 7th to 9th week onwards into levels below the normal range. All other patients had estrogen levels below the 95% confidence limits in all serum samples analyzed (Fig. 8).

DISCUSSION

In our study early pregnancies with vaginal bleeding and ultrasonic diagnosis of blighted ovum were included. In this material there were no cases with rapid spontaneous abortions without previous ultrasonic examination and there were also excluded all cases in which the ultrasound revealed typical signs of missed abortion

(fetal echoes without fetal life). A typical ultrasonic finding of an empty anembryonic gestation sac was observed in all cases at the first or subsequent examination.

In the histopathologic study of the abortive tissues there is the problem of distinguishing real pathologic changes of villi from nonspecific postmortem phenomena as well, as most specimens are incomplete, consisting only of decidual villi or only of decidua (break up of sac at evacuation?) thus making the diagnosis of blighted ovum sometimes impossible⁽⁹⁾. In the present study real pathologic changes of villi and stroma compatible with blighted ovum were found in 50% of all cases. Emmrich (1967) and Herting and Sheldon (1943) reported a corresponding frequency of 32% and 49%, respectively. Jouppila and Herva (1980) described a frequency of 55% of pathologic ova in miscarriages after a previous ultrasonic diagnosis of blighted ovum. On the contrary in 16.7% of all cases the aborted tissues had such postmortem phenomena, so that the real pathologic appearance of villi and stroma was uncertain. In the present study such doubtful cases were classified

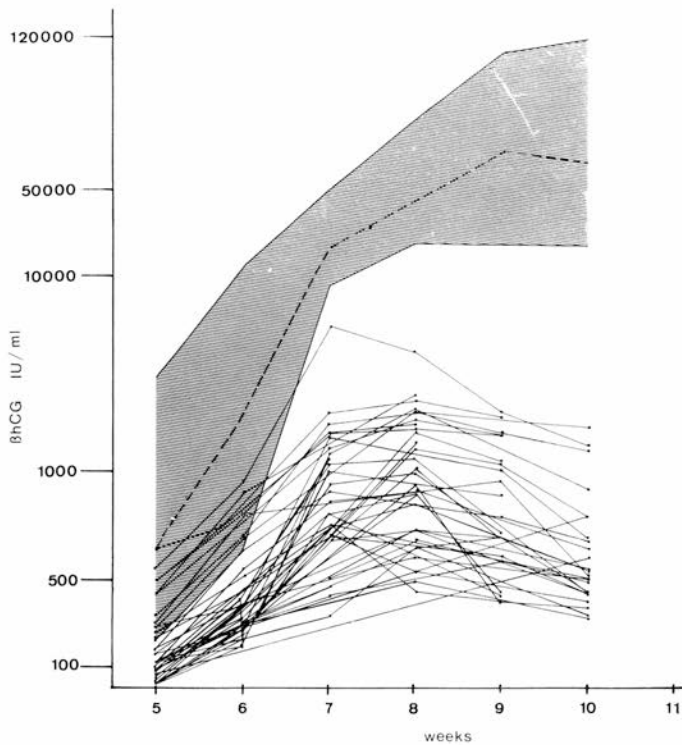


Fig. 6. — Serum hCG levels in patients having a blighted ovum: normal pregnancy range (mean \pm 1SD) is shown as hatched area.

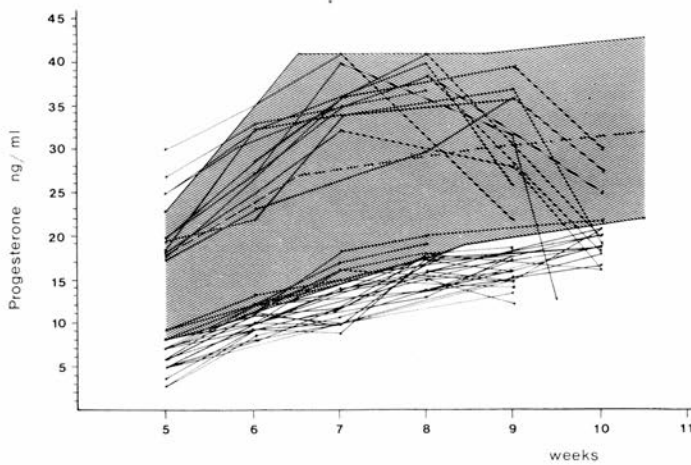


Fig. 7. — Serum progesterone (P₄) levels in patients having a blighted ovum: normal pregnancy range (mean \pm 1SD) is shown as hatched area.

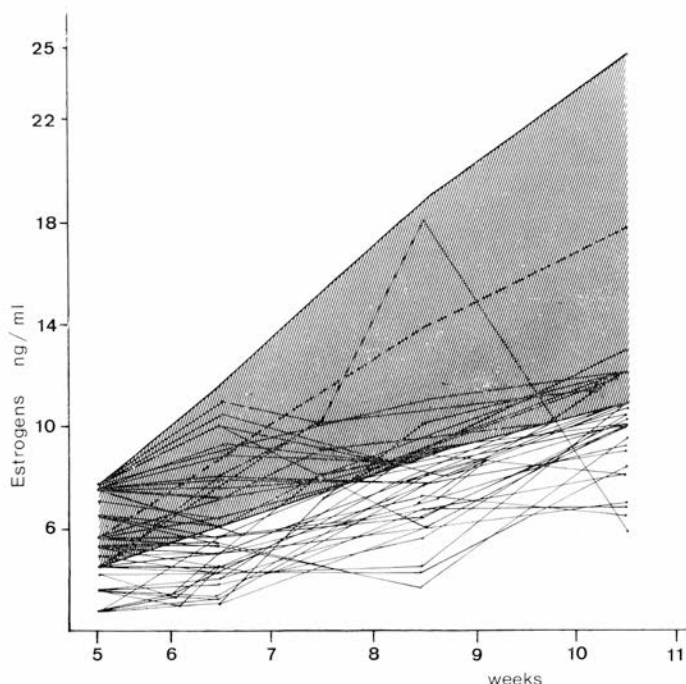


Fig. 8. — Serum estradiol (E_2) levels in patients having a blighted ovum: normal pregnancy range (mean \pm 1SD) is shown as hatched area.

as probable blighted ova. Furthermore normal villi were found in 33.3% of our patients, indicating how common the histologically normal villous tissue is in cases with absence of embryonic tissue^(9, 10).

The prediction of the later course of pregnancies complicated with bleeding still presents difficulties and hormonal determinations of hCG, E_2 , and P_4 have been used with promising and also conflicting results⁽³⁻⁵⁾. In the present study the determination of hormone patterns seems to parallel in some degree the histological observations. Serum β -hCG concentrations were low in all pregnancies throughout their gestations. Although in 8 (27%) patients normal but low β -hCG values were observed at the beginning of pregnancy (5th - 6th week) and fell only thereafter.

Plasma P_4 values were below the normal range in 18 (60%) patients and the remaining had decreased levels from the 7th to 8th week of gestation onwards. Jouppila and Herva (1980) and Schweditch *et al.* (1979) reported similar results for hCG and P_4 levels in blighted ovum pregnancies. Thus, it seems that trophoblastic tissue despite the lack of embryo has a functional capacity for a prolonged period, but the absence of the embryo per se may result in placental abnormalities.

In relation to the estrogens, we found in 46.7% of our patients normal levels of estrogens until the 9th week of pregnancy. The normal estrogen values observed during early pregnancy ought to be of maternal origin. The abnormal serum levels of estrogens observed after the 7th week of gestation could be explained by the

fact that after this time the levels are dependent upon fetal contribution which is absent in blighted ovum pregnancies (⁵).

There is a tendency for blighted ova to be retained in utero and that may lead to clinical emergencies such as bleeding and infection (^{9, 10}). Although measurements of β -hCG, E₂ and P₄ may sometimes differentiate ongoing pregnancies and blighted ova well in advance of the pregnancy miscarriage the need for reliable diagnostic methods is obvious in order to differentiate normal viable pregnancies from pathologic ova. The diagnostic reliability of ultrasonic methods from the 8th to the 10th week is of conclusive value in shortening the time of diagnostic uncertainties (^{7, 8, 10, 11}). Moreover the importance of repeated examinations must be emphasized in cases with uncertain gestational age thus eliminating the possibility of an empty gestational sac because of mistaken dates.

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