Morphological characteristics of vascular and microcirculatory disorders of the pancreas in maternal deaths from acute pancreatitis

OZODBEKOV YUSUFBEK[1], ALIBEKOV OMADBEK[2]

[1]Andijan State Medical Institute, Andijan, Uzbekistan
1 Yu. Otabekov Street, Andijan 170100, Uzbekistan
e-mail: yusufbekozodbekov571@gmail.com
ORCID: 0009-0002-9102-9580
[2]Andijan State Medical Institute, Andijan, Uzbekistan
1 Yu. Otabekov Street, Andijan 170100, Uzbekistan
ORCID: 0000-0001-8424-2784

Abstract. *Aim to identify the morphological features of damage to the vascular and microcirculatory bed of the pancreas and to assess them morphometrically in women who died of acute pancreatitis during pregnancy and the early postpartum period. Materials and methods: autopsy material from 28 women (25 pregnant, 3 postpartum) who died in 2018–2025 was examined. Haematoxylin and eosin, Van Gieson, Mallory and Weigert stains were used; morphometry was performed in 10 fields of view, comparing zones of enzymatic destruction with relatively preserved parenchyma. Results: in the destruction zones the arteriolar lumen was 2.2 times narrower (11.2 ± 1.4 vs 24.3 ± 1.8 μm), arteriolar wall thickness increased 2.2-fold, post-capillary venule diameter increased 1.9-fold, and the density of functioning capillaries decreased by 82.6% ($p < 0.001$). Perivascular oedema was found in all cases, erythrocyte stasis and sludge in 96.4%, occlusive fibrin microthrombosis in 85.7%, fibrinoid necrosis of arteriolar walls in 78.6%, and enzymatic elastolysis with vascular erosion in 67.9%. Conclusion: in fatal acute pancreatitis of pregnancy, microvascular damage is widespread and morphologically corresponds to local disseminated intravascular coagulation developing against the background of gestational hypercoagulability. The identified criteria may be used in the pathological and forensic assessment of the thanatogenesis of maternal death.*

Keywords: *pregnancy, acute pancreatitis, microcirculation, maternal mortality, disseminated intravascular coagulation, elastolysis, morphometry.*

Introduction

Acute pancreatitis (AP) during pregnancy is relatively rare; however, its severe necrotizing forms carry a high risk of maternal and perinatal death [6, 7, 10, 12]. According to current concepts, microcirculatory disorders play an important role in the progression of pancreatic necrosis: primary enzymatic injury to the acinar cells is accompanied by endothelial damage, vasoconstriction, increased vascular permeability, stasis and microthrombosis, which aggravate ischaemia and enlarge the necrotic zone [2, 3]. The close interplay of inflammation, coagulation and endothelial injury is regarded as one of the key mechanisms

in the transition of oedematous AP to its necrotizing form [3, 4].

Physiological adaptation to pregnancy is accompanied by a state of hypercoagulability: the levels of fibrinogen and coagulation factors VII, VIII, IX and X increase, while fibrinolytic activity decreases owing to elevated concentrations of plasminogen activator inhibitors types 1 and 2 (PAI-1, PAI-2) [5]. This mechanism serves to prevent massive blood loss at delivery. In acute enzymatic inflammation of the pancreas, however, activation of the kallikrein–kinin system and the release of lipase, phospholipase A2 and elastase damage the vascular endothelium and basement membranes [2, 3]. Against a background of pre-existing hypercoagulability, such injury may promote rapid intravascular coagulation, up to disseminated intravascular coagulation (DIC) [4, 5].

Although the clinical aspects of AP in pregnancy have been actively studied [6–11, 13], a detailed pathomorphological description of the pancreatic vascular bed in autopsy material from maternal deaths remains insufficiently covered in the literature.

The aim of the study was to identify the morphological features of damage to the pancreatic microcirculatory bed and to quantify vascular disorders morphometrically in maternal deaths from acute pancreatitis.

Materials and methods

A retrospective analysis was performed of autopsy material from 28 women who died of acute pancreatitis and its multiple organ complications during pregnancy (n = 25) or in the early postpartum period (n = 3) in 2018–2025. The mean age of the deceased was 27.4 ± 3.8 years (range 19–39). Distribution by gestational age: first trimester – 3 cases (10.7%), second trimester – 8 (28.6%), third trimester – 14 (50.0%), early postpartum period – 3 (10.7%). The morphological forms of pancreatitis were defined with reference to the revised Atlanta classification (2012) [1].

Autopsy material was sampled no later than 12–18 hours after the declaration of biological death. Tissue fragments measuring 1.5 × 1.0 × 0.5 cm were excised from the head, body and tail of the pancreas and from the peripancreatic adipose tissue, always including interlobular vessels and demarcation borders. The material was fixed in 10% neutral buffered formalin (pH 7.4) for 48 hours, processed through ascending concentrations of ethanol and embedded in paraffin. Serial sections 4–6 μm thick were cut on a rotary microtome.

Haematoxylin and eosin staining was used for general assessment, Van Gieson picrofuchsin staining for stromal–vascular relationships, Mallory staining for fibrin and vascular-wall collagen, and Weigert resorcin-fuchsin staining for elastic fibres and verification of elastolysis. Morphometry was performed using an Olympus BX53 microscope (Japan) and cellSens Standard software. In each case, the following were measured in 10 representative fields of view: the luminal diameter of arterioles and post-capillary venules, arteriolar wall thickness, the density of open (functioning) capillaries per 1 mm² of section area, and the proportion of thrombosed microvessels. Relatively preserved (perifocal) areas of parenchyma in the same pancreas served as an internal control.

Statistical analysis was performed in Statistica 10.0. Quantitative variables are presented as mean and standard error of the mean (M ± m); qualitative variables as absolute numbers and proportions (%) with 95% confidence intervals (CI, Wilson method). Differences were assessed with Student's t-test and the Mann–Whitney test; $p < 0.05$ was considered statistically significant.

The study was carried out on archival autopsy material in accordance with the principles of the Declaration of Helsinki; no personal data of the

deceased were included in the analysis.

Results

Pathomorphological analysis showed that in all cases the vascular bed of the pancreas was profoundly disorganized, with changes involving every level of the microcirculation – arterioles, precapillaries, capillaries, post-capillaries and venules. The morphometric findings are presented in Table 1.

Table 1. Morphometric parameters of the pancreatic microcirculatory bed (M ± m)

Morphometric parameter	Relatively preserved zones (internal control)	Zones of enzymatic destruction	p
Arteriolar lumen, μm	24.3 ± 1.8	11.2 ± 1.4 (spasm/collapse)	< 0.001
Arteriolar wall thickness, μm	5.8 ± 0.4	12.6 ± 0.9 (oedema/fibrinoid)	< 0.001
Post-capillary venule diameter, μm	38.6 ± 2.5	74.5 ± 4.1 (dilatation/stasis)	< 0.001
Density of functioning capillaries, per mm²	184.2 ± 12.3	32.1 ± 4.6 (reduction of the bed)	< 0.001
Proportion of thrombosed microvessels, %	4.2 ± 0.8	78.6 ± 5.2 (microthrombosis)	< 0.001

As shown in Table 1, in the destruction zones the arteriolar lumen narrowed 2.2-fold (to 11.2 ± 1.4 μm), while arteriolar wall thickness increased 2.2-fold (to 12.6 ± 0.9 μm) owing to plasma insudation and swelling of the basement membranes. The density of functioning capillaries fell from 184.2 ± 12.3 to 32.1 ± 4.6 per mm², i.e. by 82.6%, indicating marked tissue hypoperfusion (Fig. 1).

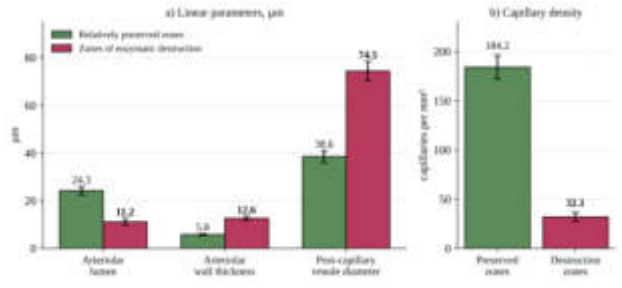


Figure 1. Morphometric parameters of the pancreatic microcirculatory bed in relatively preserved zones and zones of enzymatic destruction (M ± m; p < 0.001 for all parameters)

Weigert staining revealed segmental and diffuse elastolysis in small arteries and arterioles: the internal elastic lamina lost its undulation, fragmented and in places disappeared completely, which was attributed to the action of pancreatic elastase. In the zones of elastolysis the vessel wall became thinned, with formation of microaneurysms and subsequent erosion. In our view, these changes underlay the massive interstitial haemorrhages and the development of haemorrhagic pancreatic necrosis. The frequency of vascular and haemorheological disorders is shown in Table 2.

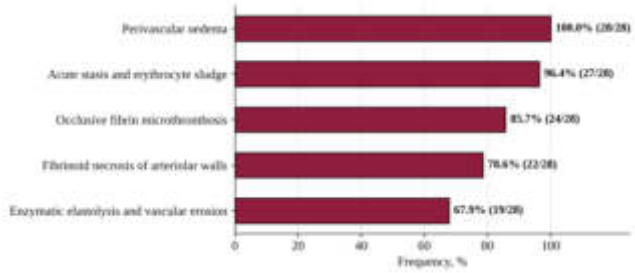


Figure 2. Frequency of vascular and haemorheological disorders in fatal acute pancreatitis in pregnancy (n = 28)

Paralytic congestion was observed at the venular level: the diameter of post-capillary venules almost doubled (74.5 ± 4.1 vs 38.6 ± 2.5 μm). Their lumens contained dense

erythrocyte aggregates (sludge – 96.4%) and occlusive fibrin microthrombi (85.7%). Perivascular oedema, present in all cases, compressed the thin-walled venules, increasing venous hypertension and erythrocyte diapedesis.

Table 2. Frequency of vascular and haemorheological disorders in fatal acute pancreatitis in pregnancy (n = 28)

Pathomorphological finding	n	% (95% CI)	Pathogenetic significance
Perivascular serous-haemorrhagic oedema	28	100.0 (87.9–100.0)	Interstitial hypertension, compression of venules
Acute stasis and erythrocyte sludge	27	96.4 (82.3–99.4)	Rheological blockade of capillaries, tissue hypoxia
Occlusive fibrin microthrombosis	24	85.7 (68.5–94.3)	Organ manifestation of local DIC
Fibrinoid necrosis of arteriolar walls	22	78.6 (60.5–89.8)	Irreversible damage to the vessel wall, loss of tone
Enzymatic elastolysis and vascular erosion	19	67.9 (49.3–82.1)	Morphological substrate of massive haemorrhage

Discussion

Our findings are consistent with the concept of the leading role of microcirculatory disorders in the progression of acute pancreatitis, formulated mainly on the basis of experimental and clinical studies [2, 3]. The combination of arteriolar vasoconstriction, capillary rarefaction, venular stasis and microthrombosis observed here corresponds to the elements of the "microcirculatory" pathogenesis of pancreatic necrosis described in the literature – endothelial dysfunction, increased permeability and activation of coagulation [3, 4].

The high frequency of fibrin microthrombi (85.7%) and sludge (96.4%) in our material may be explained by enzymatic endothelial injury superimposed on the physiological hypercoagulability of pregnancy, in which the levels of fibrinogen, procoagulant factors and fibrinolysis inhibitors are markedly increased [5]. Pregnancy is regarded as a state of heightened susceptibility to DIC [5], and haemostatic disturbances in severe AP are well recognized [4]. Taken together, the observed changes allow the morphogenesis of vascular injury to be represented as a self-sustaining vicious circle: enzymaemia (elastase, trypsin) → endothelial damage and elastolysis of the arteriolar wall → microthrombosis against the background of gestational hypercoagulability (local DIC) → acinar ischaemia → secondary necrosis of the gland → endotoxaemia and multiple organ dysfunction syndrome.

The predominance of fatal cases in the third trimester (50.0%) agrees with clinical series in which AP in pregnancy develops more often in late gestation [6, 9, 11]; it is in this period that hypercoagulable changes are most pronounced [5].

Limitations. The study was based on a limited retrospective autopsy series without an external control group (non-pregnant women with AP); relatively preserved zones of the same gland were used as the control. Antemortem haemostatic parameters were not analysed, which precludes direct comparison of the morphological changes with laboratory criteria of DIC. The possible influence of postmortem changes on morphometric parameters was minimized by the timing of

sampling (no later than 12–18 h).

Conclusions

1. An important morphogenetic element of thanatogenesis in fatal acute pancreatitis in pregnancy is widespread damage to the microcirculatory bed: enzymatic elastolysis, fibrinoid necrosis of arteriolar walls (78.6%) and an 82.6% reduction of the functioning capillary network.

2. Physiological gestational hypercoagulability under conditions of enzymatic aggression is accompanied by morphological signs of local DIC – occlusive microthrombosis (85.7%) and erythrocyte sludge (96.4%).

3. The qualitative and morphometric parameters of vascular injury identified here may serve as objective criteria in the pathological and forensic assessment of the severity and tempo of thanatogenesis in maternal death, and support further study of early prevention of thrombohaemorrhagic complications in pregnant women with acute pancreatitis.

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