Histological and Immunohistochemical Study on the Possible Relationship between experimentally Induced Acute Pancreatitis and its Associated Lung Injury

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Abstract

Introduction: Acute pancreatitis is an inflammatory process with very high morbidity and mortality rate. It may be complicated with multiorgan failure. Pulmonary complications are the most frequent and potentially the most serious complications

Aim of the work: To elucidate the possible relationship between L-arginine induced acute pancreatitis and its associated lung injury in adult male albino rats by using histological and immunohistochemical techniques.

Materials and methods: This study was performed on fourteen adult male albino rats. Animals were randomly divided into two groups: Group I (Control group), which were given two intraperitoneal injections of normal saline, 1 h apart, Group II (Acute pancreatitis group (AP) in which pancreatitis was induced by two intraperitoneal injections of L-arginine, 1 h apart. Histological (using H&E) immunohistochemical (using anti TNF-α, anti IL-6 and anti P-selectin) studies were performed. Moreover, morphometric study followed by statistical analysis were done for area % of TNF-α, IL-6 and P-selectin immunoexpression in pancreatic and lung tissues.

Results: AP group revealed inflammatory cellular infiltration within the connective tissue septa of the pancreas. The lungs of AP group showed thickened interalveolar septa with massive inflammatory cellular infiltration. A significant increase in immunoreactivity of TNF-α, IL-6 and P-selectin in pancreatic and lung tissues was observed.

Conclusion: The present study shed the light on the important role of TNF-α, IL-6 and P-selectin in the pathogenesis of acute pancreatitis and its associated lung injury

Keywords: Acute pancreatitis, Lung injury, L-arginine, TNF-α, IL-6, P-selectin

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Introduction

Acute pancreatitis (AP) is an acute inflammatory process of the pancreas ***(Fisher et al., 2010)***. The pathomechanisms of AP is poorly understood. Therefore, AP is still associated with significant mortality and morbidity ***(Bulut et al., 2011)***. Sever pancreatitis is complicated by the development of multiorgan dysfunction syndrome. Pulmonary complications are one of these systemic complications. They are the most frequent and potentially the most serious complications. Recognition of these complications and their pathogenesis may pave the way for more rapid iagnosis and finding out better therapeutic strategies ***(Kylanpaa et al. 2010).***

Alcohol and gall stones are two major etiological factors responsible for acute pancreatitis.The proportions of pancreatitis attributed to alcohol and gall stones vary significantly in different countries and regions ***(Whitcomb, 2006).*** 10% of all cases of pancreatitis are idiopathic and no causative factor can be known ***(Guda et al. 2011).***

L-arginine has been used by athletes to enhance production of human growth hormone. The effects of arginine supplementation include increased fat burning and muscle building, enhanced immunity, and improvement in erectile function. Recent studies have demonstrated that excessive doses of arginine induce necrotizing pancreatitis in rats. In one case report, a 16-year-old male patient hospitalized due to severe pain in upper abdomen, nausea and vomiting. L-arginine-induced acute pancreatitis was diagnosed ***(Saka et al., 2004; and Saluja, 2012).***

Previous studies have shown that inflammatory cytokines play an important role in the induction and severity of AP. Clinical and experimental studies have shown that serum tumour necrosis factor-α (TNF-α) and some interleukins (IL) are increased in patients with AP. These inflammatory cytokines expressed by activated macrophages, locally increase the severity of AP ***(Shivastava and Bhatia, 2010; Kylnappa et al., 2010)***. The inflammatory response is initiated by injured pancreatic acinar cells that produce inflammatory mediators, such as cytokines (e.g., TNF-α, IL6) and adhesion molecules (e.g., P-selectin), ultimately leading to systemic complications ***(shen et al., 2011; Hackert et al, 2010).***

The aim of this work was to elucidate the possible pathomechanisms of L-arginine induced acute pancreatitis and its associated lung injury in adult male albino rats by using histological and immunohistochemical techniques.

Materials and Methods

Animals

Fourteen adult male albino rats, locally bred at the Animal House of Kasr El Aini with an average weight of 200-250 gm were used in the present study. The animals were housed at ordinary room temperature, exposed to natural daily light-dark cycles, had access to food and water *ad libitum*. This study has been approved by the ethics committee for animal research in the animal house of Kasr-El-Aini Faculty of Medicine, Cairo University, Egypt following international ethics and regulations for animal research in laboratory applications ***(Gluck et al., 2002).***

Experimental design

The animals were divided into two groups:

Group I: (Control group)

Included seven rats which were given two intraperitoneal injections of normal saline, 1 h apart at the same time of the corresponding experimental group.

Group II: (Acute pancreatitis (AP) group)

Included seven rats which were injected intraperitoneally with L-Arginine (Sigma-Aldrich, St. Louis, MO, USA) in two doses of 2 g/kg body weight each, 1 h apart ***(Chen et al., 2012).***

Sample collection

After 3 days, the rats were anesthetized using injection of thiopental sodium 50 mg/ kg subcutaneously and then sacrificed. The pancreas and lungs were dissected and fixed in 10% formalin solution. Specimens were dehydrated, processed to obtain paraffin blocks. Five μm sections were cut and stained with H&E stain. Immunohistochemical staining was done using anti TNF-α (Abcam, Massachusetts, USA) (rabbit polyclonal antibody, code no. ab6671, the reaction is cytoplasmic and membranous and the +ve control was dendritic cells), anti IL6 (Abcam, Massachusetts, USA) (mouse monoclonal antibody, code no. ab9324, the reaction is cytoplasmic and the +ve control was human cervical squamous cell carcinoma tissue) and anti P-selectin (Abcam, Massachusetts, USA) (rabbit monoclonal antibody, code no.

ab178424, the reaction is membranous and the +ve control was the human vessel).

Morphometric study

The data were obtained using the image analyzer computer system (Leica Qwin 500, England). The area % of TNF-α, IL6 and P-selectin immunoexpression were measured in 10 high power non overlapping fields in each specimen using binary mode.

Statistical analysis

Data were expressed as group means ± SD. The statistical analysis was carried out using t- test, with SPSS version 10 (SPSS, Chicago, IL, USA). A value of $p \leq 0.05$ was accepted as statistically significant.

Results

Histological and immunohistochemical study

Pancreas

Examination of H&E-stained sections of the control pancreatic specimens showed the characteristic appearance of pancreatic acini with apical acidophilic granules and basal basophilia. A lightly stained islets of Langerhans were seen in between (Figs. 1a &b). The specimens from the AP group revealed congested blood vessels, distortion and vacuolation of pancreatic acini (Figs. 2a & b). They also demonstrated extravasation of

RBCs and infiltration of mononuclear inflammatory cells in the connective tissue septa in some specimens (Figs. 3a & b).

TNF-α immuno-stained sections of control pancreas demonstrated negative immunoexpression in the islets of Langerhans and the acini (Fig. 4). While AP group showed weak immunoreactivity in the islet of Langerhans and strong cytoplasmic immunoreativity in the acini (Fig. 5).

IL6 immuno-stained sections of control pancreas revealed negative immunoexpression in the islets of Langerhans and the acini. While, pancreatic ducts showed positive immunoexpression (Fig. 6). While AP group showed strong cytoplasmic immunoreativity in the acini and a weak immunoreactivity in the islet of Langerhans (Fig. 7).

P-selectin immuno-stained sections of control pancreas showed negative immunoexpression in the acini and blood vessel (Fig. 8). While, in AP group, there was strong membranous immunoreativity in the endothelium of the blood vessels and lining epithelium of pancreatic ducts. Mild immunoreactivity in the acini was observed in some specimens (Fig. 9). Many other specimens demonsrated strong immunoexpression in the acini (Fig.10).

Lung

The H&E-stained sections of control lung specimens showed normal-appearing lung architecture with the expanded alveoli separated by thin interalveolar septa and members of the bronchial tree in between (Fig. 11). Lung specimens from the AP group demonstrated edematous thickened interalveolar septa and dilated congested blood vessels with acidophilic

hyaline exudate. There was also acidophilic material with cellular debris in bronchiolar lumen. (Figs. 12, 13). Thickened and obliterated blood vessels in addition to collapsed alveoli were observed (Fig. 14).

TNF-α immuno-stained sections of control lung specimens demonstrated negative immunoexpression in the epithelial cells lining the expanded alveoli as well as in the cells of connective tissue septa (Fig. 15). The lungs of the AP group were characterized by the presence of positive immunoreactivity in the epithelial cells lining the alveoli, as well as cells present within the thickened interalveolar septa (Fig. 16).

IL6 immuno-stained sections of control lung revealed negative immunoexpression within the epithelial cells lining the expanded alveoli as well as in the cells of connective tissue septa and bronchiol (Fig. 17). While AP group showed positive cytoplasmic immunoreativity in the epithelial lining of alveoli, bronchiole and cells present within the thickened interalveolar septa (Fig. 18).

P-selectin immuno-stained sections of control lung showed negative immunoexpression in the alveoli, bronchiol, connective tissue septa and surrounding blood vessel (Fig. 19). While, in AP group, there were strong membranous immunoreativity in the wall of the blood vessels and bronchiols. Mild immunoreactivity in the alveoli and connective tissue septa (Fig. 20).

Morphometric results

A significant increase ($P \leq 0.05$) in the mean area % of TNF-α, IL6 and P-selectin immunoexpression in pancreatic and lung specimens were found in AP group compared with the control group (Table: 1).

Table:

Mean area % of TNF-α, IL6 and P-selectin immuno -expression

Groups	Control Pancreas	Experimental Pancreas	Control Lung	Experimental Lung
Mean±SD area% of TNF-α	**0.6 ± .02**	**12 ± .9**	**0.23 ± 0.1**	**10 ± 1.6**
Mean±SD area% of IL6	**1 ±.07**	**18 ± 1.53**	**0.12± 0.01**	**8 ± 2.2**
Mean±SD area% of P-selectin	**0.5 ± .12**	**8 ± 1.3**	**0.03± 0.002**	**4 ±2.1**

*$P \leq 0.05$, significant difference compared to control

Discussion

Different animal models of experimental acute pancreatitis have been induced by caerulein, choline deficient ethionine supplemented (CDE) diet, or sodium taurocholate. These models vary in severity and have been used by the researchers to either understand the pathogenesis of the disease or to study the effect of different therapeutic agents **(Zhao et al., 2013).**

Mizunuma et al. (1984) were first researchers who reported that intra-peritoneal administration of excessive doses of L-arginine (500 mg/100 g body weight) in rats selectively damage pancreatic acinar cells without any morphological change in islets of Langerhans or other organs. The mechanism of L-arginine induced pancreatitis is not clear. Arginine may be a causative agent of acute pancreatitis in human as reported by ***(Saka et al., 2004).*** So, physicians must keep this in mind.

Acute hemorrhagic necrotizing pancreatitis (AHNP) is a potentially fatal disease with very high morbidity and mortality rate. Acute lung injury (ALI) is a common complication of AHNP, but the interorgan signals that link AHNP and pulmonary damage are not fully understood. Many factors, such as oxygen free radicals, platelet activating factor, phospholipase A_2 (PLA_2), cyclooxygenase-2 (COX-2), cytokines and arachidonic acid metabolites may

be related to AHNP and ALI ***(Liu et al., 2006; Gravante et al., 2009).***

The choice of examining the specimens after 72 hs in AP group exposed to L-arginine, was based on a study of ***Chen et al. (2012)*** that declared that the peak injury occurred after 72 hs.

In the present study, examination of H & E stained pancreatic sections of AP group showed congested blood vessels, acinar necrosis in the form of distortion and vacuolation of pancreatic acinar cells. They also demonstrated extravasation of RBCs (hemorrhage) and infiltration of mononuclear inflammatory cells within the dilated connective tissue septum. These results were in accordance with ***Chen et al. (2012)*** who demonstrated pancreatic interstitial edema, neutrophil infiltration, hemorrhage, and acinar cell necrosis in the pancreas, with peak injury occurring after 72 h, and without any morphological changes in the Langerhans islets. ***Wang et al. (2012)*** also revealed severe form of AP by retrograde perfusion into the biliopancreatic duct of 3.5% sodium taurocholate which was characterized by expansion of interlobular spaces caused by moderate to severe interstitial edema, extensive infiltration with inflammatory cells, obvious pancreatic acinar cells vacuolization, necrosis and hemorrhage. ***Buyukberber et al. (2009), Sidhapuriwala et al. (2012) & Safinaz and Dina (2013)*** have shown the same results but by using different methods for inducing pancreatitis and different times of scarification.

Worth mentioning is that under normal conditions, digestive enzymes and enzyme precursors known as zymogens are packed into zymogen granules. These granules release their contents into the pancreatic duct after eating. In

pancreatitis, a decrease in secretion to the duodenum in animals and humans is noted. This is due to decreased apical secretion of the acinar cells, disruption of the paracellular sealing in the pancreatic duct. These events allow the contents to leak into the paracellular space and redirect the secretion of the zymogen granules from the apical pole to the basolateral regions of the acinar cell, as shown by in-vitro and in-vivo animal studies ***(Gaisano & Gorelick 2009).***

Previous studies have shown that neutrophils and leukocytes were attracted to the site of an injury as early as 3 hours after induction of pancreatitis ***(Shanmugam & Bhatia, 2010).*** Infiltrating polymorphonuclear neutrophils produce oxygen-free radicals and thus cause local and systemic complications ***(Beger et al., 2000).*** Monocytes and macrophages have an important role in the pathogenesis of acute pancreatitis. They migrate to the pancreatic interstitium from the circulation ***(Shirivastava et al., 2008).*** They also produce cytokines and other inflammatory mediators ***(Shrivastava & Bhatia, 2010).*** The degree of monocyte activity may be related to disease severity and thus the degree of local damage ***(Liang et al., 2008).***

A significant increase in immunoreactivity of TNF-α, IL6 and P-selectin (represented by area %) was observed in AP group compared with the control group. There are a few previous works concerning the presence of cytokines in pancreatitis 6 to 72 hours following the onset of the disease. TNF-α and IL-6 have all been shown to rise in serum after 6 to 24 hours of severe acute pancretitis ***(Yekebas et al., 2002; Yang et al., 2004; Gulcubuk et al., 2006; Feng et al., 2012)***. ***Sidhapuriwala et al. (2012)*** demonstrated upregulation of TNF-α, IL-6 in pancreatic and lung tissues using ELIZA.

Koh et al. (2011) revealed upregulation of TNF-α, IL-6 and P-selectin in pancreatic tissue by ELISA assays. ***Joo et al. (2009)*** also demonstrated increased immunoexpression of TNF-α by immunohistochemistry. A previous study done by ***Folch et al. (1999) and Hartman et al. (2012)*** demonsrated markedly increased P-selectin immunoexpression in the pancreas after pancreatitis induction.

Several cytokines have been found to be associated with the pathogenesis of Pancreatitis. These include a pro-inflammatory cytokine: tumour necrosis factor-α (TNF-α), interleukin- 6 (IL-6). IL-6 is also an important anti-inflammatory cytokine. It can act as anti-inflammatory cytokine as well ***(Kylanpaa et al., 2010, Kilciler et al., 2008, Shen et al., 2011 and Hayashi et al., 2007).*** TNF-α is produced by blood monocytes and macrophages. It mediates the release of various inflammatory mediators and has a strong toxic effect. Interleukin-6 (IL-6) is one of the most studied cytokines and chemokines in acute pancreatitis. It has been shown to possess an early prognostic value for the severity of the disease. Till now, it has limited clinical use ***(Aoun et al., 2009).***

IL-6 is an atypical cytokine that has both pro- and anti-inflammatory effects. The proinflammatory effect of IL-6 is suggested by the concomitant increase in the levels of IL-1β and TNF-α. IL-1β and TNF-α are known to induce the production of IL-6. Thus, IL-6 can perpetuate the inflammatory response to infection. However, the level of IL-6 increased on day 5, similar to the levels of other anti-inflammatory cytokines (IL-4 and IL-10). This may indicate its dual role (***Clahsen & Schaper, 2008; Nadia et al., 2008)***.

P-selectin is a glycoprotein mediating the adhesion of activated platelets and leukocytes to the vessel wall in various inflammatory conditions. P-selectin in AP has a dual function, a mediator of leukocyte recruitment and cell adhesion. This implies the unique effect of linking both inflammation and coagulation; especially in the progression from mild to severe necrotizing AP. Overproduction of inflammatory cytokines in AP induces expression of adhesion molecules. This may lead to increased leukocytic infiltration and tissue damage ***(Hackert et al., 2010).***

The present work revealed many morphological changes in H & E stain lung specimens of AP group. It demonstrated edematous thickened interalveolar septa and dilated congested blood vessels with acidophilic hyaline exudate. There was also acidophilic material with cellular debris in bronchiolar lumen. Mononuclear inflammatory cellular infiltrate was noticed inside the lumen of bronchioles and in the thickened interalveolar septa. Thickened and obliterated blood vessels in addition to collapsed alveoli were observed. The previous findings were concomitant with that of ***Chen et al. (2012)*** who revealed inflammatory cell infiltration (predominantly neutrophils), pulmonary edema, and hemorrhage of alveoli and interstitial tissue. Other previous studies have shown similar findings ***(Sidhapuriwala et al., 2012; Safinaz and Dina, 2013 and Zhang et al. 2013).***

Furthermore, there were significant increase in immunoreactivity of TNF-α, IL6 and P-selectin (represented by area %) in AP group as compared with the control group. This was in agreement with ***Koh et al. (2011)*** who revealed upregulation of TNF-α, IL-6 and P-selectin in lung tissue by ELISA assays. ***Sidhapuriwala et al. (2012)*** also demonstrated upregulation of TNF-

α, IL-6 in pancreatic and lung tissues using ELIZA. ***Yubero et al. (2012)*** showed up-regulation of lung mRNA expression of P-selectin.

The pathophysiology of Sever acute pancreatitis with acute lung injury is poorly understood. Researchers have hypothesized that during localized inflammation; Cytokines may leak into the circulation and exceed the amount of soluble receptors, which may then lead to systemic inflammation ***(Castellheim et al., 2009).***

In acute pancreatitis, pro-inflammatory cytokines secreted from the pancreatic cells, vascular endothelial cells and tissue macrophages in the pancreas, enter the circulation through the portal vein and the lymphatic system. They activate the vascular endothelium leading to micro-vascular leakage of the capillary veins and leukocyte migration into the tissues, as seen in experimental rat pancreatitis. Proinflammatory cytokines also activate the coagulation process in human patients which causes thrombosis in the small vessels of many organs. Both of these phenomena result in impaired tissue microcirculation. Thus, it may lead to organ failure in severe pancreatitis ***(Kylanpaa et al., 2010).***

So, changes occuring in acute lung injury involve endothelial barrier dysfunction, neutrophil and monocyte/macrophage activation, adhesion molecule expression and intracellular signaling. These can be executed by proteases derived from polymorphonuclear neutrophils (PMNs). This process seems driven by tumor necrosis factor (TNF)-α and monocyte chemoattractant protein (MCP)-1, with involvement of mast cells, at least

during the initiation of leukocyte activation. So, it seems that inflammatory mediators may play a key role in the pathogenesis of ALI. These mediators include TNF-α, interleukins-1β, -6, and -10, transforming growth factor-β, granulocyte-macrophage colony-stimulating factor, platelet-activating factor (PAF), selectin and adhesion molecules, complement component C5a, neuropeptide substance P, and chemokines such as MCP-1, and macrophage inflammatory protein-1α. Moreover, production of reactive oxygen and nitrogen species may also have a role by triggering the expression of P-selectin. Moreover, Active pancreatic enzymes in circulation, released as a result of pancreatic injury, play a key role in the development of pulmonary complications of pancreatitis ***(Browne and Pitchumoni, 2006 & Zhou et al., 2010).***

Conclusion

The findings of the present study shed the light on the important role of some cytokines and adhesion molecules like TNF-α, IL-6 and P-selectin in the pathogenesis of acute pancreatitis and its associated lung injury. Also, arginine may be a causative agent of acute pancreatitis

Recommendations

Further studies are required for deeper understanding of the cell biology and physiology of AP to permit the design of effective interventions concerning the inflammatory response process. More studies done on the consequences of arginine are required as it's widely used by many bodybuilders

Legends

Figs. 1a, b: photomicrographs of a section of a rat pancreas in group I (control group) showing the characteristic appearance of pancreatic acini (thin arrows) with apical acidophilic granules and basal basophilia. A lightly stained islets of Langerhans (thick arrows) were seen in between.

a- Hx. &E., x 100

b-Hx. &E., x 400

Figs. 2a, b: photomicrographs of a section of a rat pancreas in group II (AP group) showing congested blood vessels (thick arrow), distortion and vacuolation of pancreatic acini (thin arrows).

a- Hx. &E., x 100

b-Hx. &E., x 400

Figs. 3a,b: photomicrographs of a section of a rat pancreas in group II (AP group) showing extravasation of RBCs (curved arrows) and infiltration of mononuclear inflammatory cells (dashed arrows) in the connective tissue septum.

a- Hx. &E., x 100

b-Hx. &E., x 400

Fig. 4: A photomicrograph of a section of a rat pancreas in group I (control group) showing negative immunoexpression in the islets of Langerhans (thick arrows) and the acini (thin arrows).

TNF-α immunostain x 400

Fig. 5: A photomicrograph of a section of a rat pancreas in group II (AP group) showing strong cytoplasmic immunoreativity in the acini (thin arrows) and weak immunoreactivity in the islets of Langerhans (thick arrows).

TNF-α immunostain x 400

Fig. 6: A photomicrograph of a section of a rat pancreas in group I (control group) showing negative immunoexpression in the islets of Langerhans (thick arrows) and the acini (thin arrows). A positive cytoplasmic immunoexpression is noticed in a pancreatic duct (crossed arrows).

IL-6 immunostain x 400

Fig. 7: A photomicrograph of a section of a rat pancreas in group II (AP group) showing strong granular cytoplasmic immunoreativity in the acini (thin arrows). A weak immunoreactivity in the islet of Langerhans (thick arrows) is observed.

IL-6 immunostain x 400

Fig. 8: A photomicrograph of a section of a rat pancreas in group I (control group) showing negative immunoexpression in the acini (thin arrows) and a blood vessel (curved arrows).

P-selectin immunostain x 400

Fig. 9: A photomicrograph of a section of a rat pancreas in group II (AP group) showing strong membranous immunoreativity in the endothelium of the blood vessels (curved arrows) and lining epithelium of pancreatic ducts (crossed arrows).

P-selectin immunostain x 400

Fig. 10: A photomicrograph of a section of a rat pancreas in group II (AP group) showing strong immunoexpression in the acini (arrows).

P-selectin immunostain x 400

Fig. 11: A photomicrograph of a section of a rat lung in group I (control group) showing normal-appearing lung architecture with the expanded alveoli separated by thin interalveolar septa (thin arrows) and members of the bronchial tree in between (thick arrows).

Hx. &E., x 100

Fig. 12: A photomicrograph of a section of a rat lung in group II (AP group) showing edematous thickened interalveolar septa (thin arrows) and dilated congested blood vessels (dotted arrows) with acidophilic hyaline exudate (curved arrows). There is also acidophilic material with cellular debris in bronchiolar lumen (thick arrows).

Hx. &E., x 100

Fig. 13: A photomicrograph of a section of a rat lung in group II (AP group) showing mononuclear inflammatory cellular infiltrate inside the lumen of a bronchiole (dotted arrows) and in the thickened connective tissue septa (double headed arrows).

Hx. &E., x 400

Fig. 14: A photomicrograph of a section of a rat lung in group II (AP group) showing thickened and obliterated blood vessels (thick arrows) in addition to collapsed alveoli (thin arrows).

Hx. &E., x 100

Fig. 15: A photomicrograph of a section of a rat lung in group I (control group) showing negative immunoexpression within the epithelial cells lining the expanded alveoli (thin arrows) as well as in the cells of connective tissue septa (thick arrows).

TNF-α immunostain x 400

Fig. 16: A photomicrograph of a section of a rat lung in group II (AP group) showing positive immunoreactivity within the cytoplasm of the epithelial lining of the alveoli (thin arrows), as well as cells present within the thickened interalveolar septa (thick arrows).

TNF-α immunostain x 400

Fig. 17: A photomicrograph of a section of a rat lung in group I (control group) showing negative immunoexpression within the epithelial cells lining the expanded alveoli (thin arrows) and a bronchiole (thick arrows).

IL-6 immunostain x 400

Fig. 18: A photomicrograph of a section of a rat lung in group II (AP group) showing positive cytoplasmic immunoreativity in the epithelial lining of alveoli (thin arrows), bronchiole (thick arrows) and cells present within the thickened connective tissue septa (double headed arrows).

IL-6 immunostain x 400

Fig. 19: A photomicrograph of a section of a rat lung in group I (control group) showing negative immunoexpression in the alveoli (thin arrows), bronchiol (thick arrows), connective tissue septa (double headed arrows) and the blood vessels (dotted arrows).

P-selectin immunostain x 400

Fig. 20: A photomicrograph of a section of a rat lung in group II (AP group) showing strong membranous immunoreativity in the blood vessel (dotted arrows) and a bronchiol (thick arrows). Mild immunoreactivity in the alveoli (thin arrows) and connective tissue septa (double headed arrows).

P-selectin immunostain x 400

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الملخص العربى

دراسة هستولوجيه وهستوكيميائية مناعيه حول العلاقة المحتملة بين التهاب البنكرياس الحاد المحدث تجريبيا و إصابة الرئة المرتبطه به

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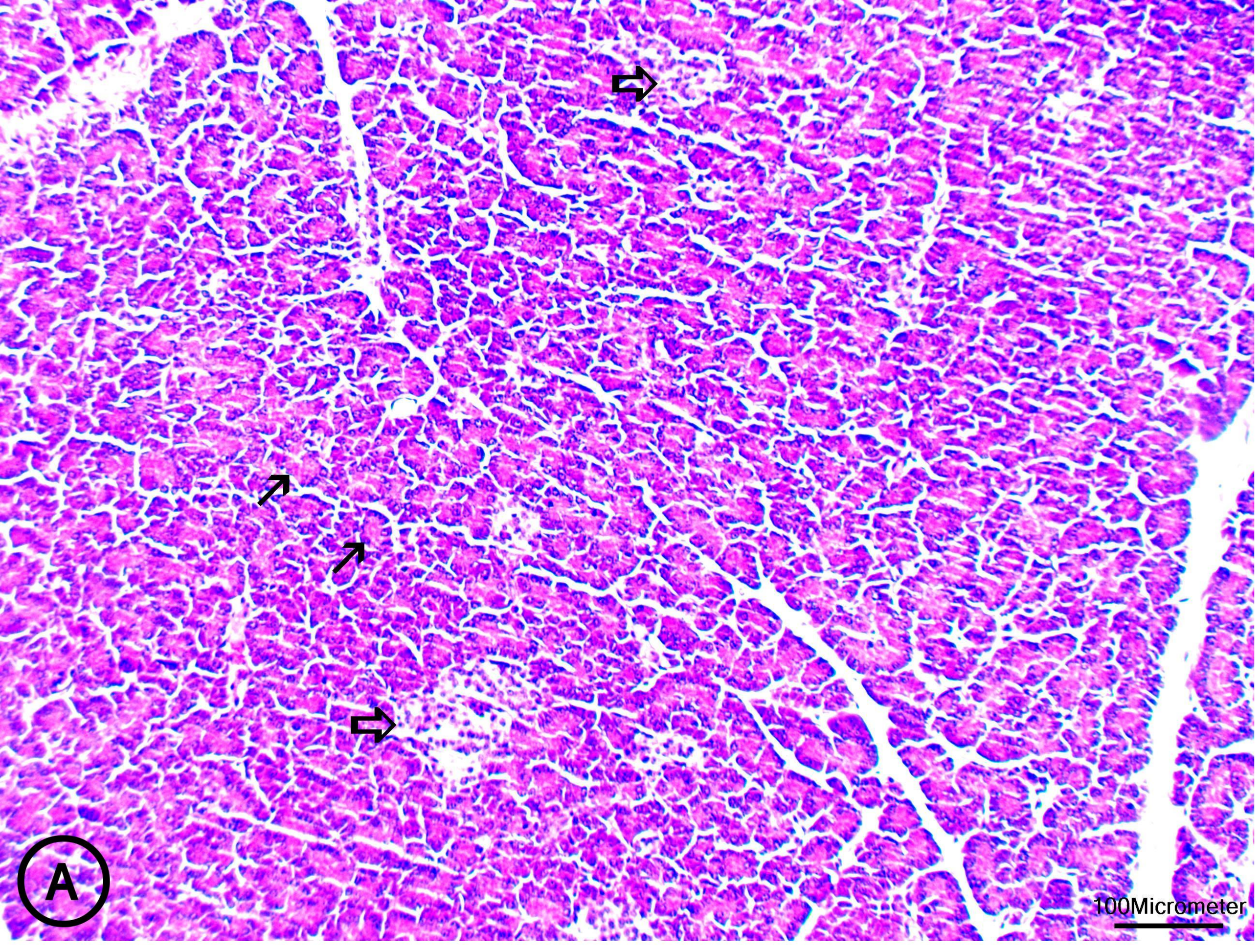
مقدمة: التهاب البنكرياس الحاد هو عملية التهابية مع معدل مرضى ووفيات عالي جدا. وربما يصاحبه مضاعفات مع فشل أعضاء متعدد. المضاعفات الرئوية هي المضاعفات الأكثر شيوعا والاكثر خطورة.

الهدف من البحث: لتوضيح العلاقة المحتمله بين التهاب البنكرياس الحاد والإصابة المرتبطة في الرئة المحدثه بواسطة عقار الارجنين في ذكور الجرذان البيضاء البالغة باستخدام التغيرات الهستولوجيه والهستوكيميائية مناعيه .

المواد وطرق البحث:_هذه الدراسة قد أجريت على أربعة عشر من ذكور الجرذان البيضاء البالغة. قسمت الحيوانات عشوائيا إلى مجموعتين: المجموعة الأولى (المجموعة الضابطة)، والتي أعطيت حقنتين داخل الغشاء البريتونى من محلول ملح عادي، يفصل بينهما ساعه، المجموعة الثانية (مجموعة التهاب البنكرياس الحاد (AP) حيث احدث التهاب البنكرياس بواسطة حقنتين داخل الغشاء البريتونى لعقار L-أرجينين، يفصل بينهما ساعة. وقد أجريت دراسات هستولوجية (باستخدام صبغات الهيماتوكسلين) وهستوكيميائية مناعية (باستخدام مضاد TNF-α ، و مضاد IL-6 ومضاد P-selectin). وعلاوة على ذلك، تم عمل قياسات التحليل المصور اتبعت بالتحليل الاحصائى للمساحة المئوية ل TNF-α, IL-6 and P-selectin فى انسجة البنكرياس والرئة.

النتائج: كشفت مجموعة AP تسلل خلايا التهابيه داخل حواجز النسيج الضام في البنكرياس. أظهرت الرئتين من مجموعة AP زيادة سمك الحاجز بين الحويصلات مع تسلل كبير للخلايا الإلتهابيه. و قد لوحظ زيادة كبيره في التفاعل المناعى ل TNF-α، IL-6 و P-selectin في أنسجة البنكرياس والرئة. .

الخلاصة: تسلط هذه الدراسة الضوء على الدور الهام لل TNF-α ، IL-6 و P-selectin في التسبب في التهاب البنكرياس الحاد وإصابة الرئة المرتبط به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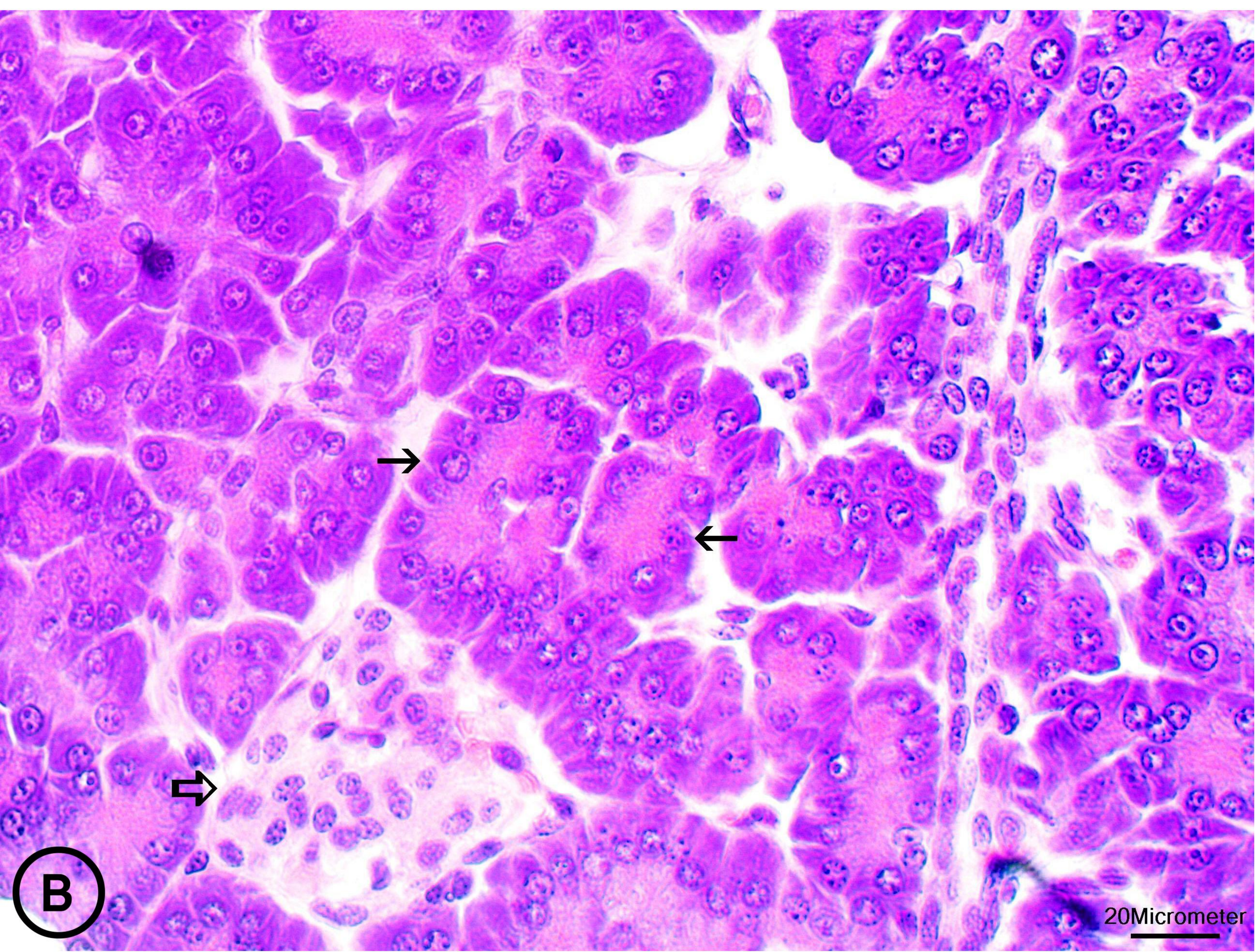
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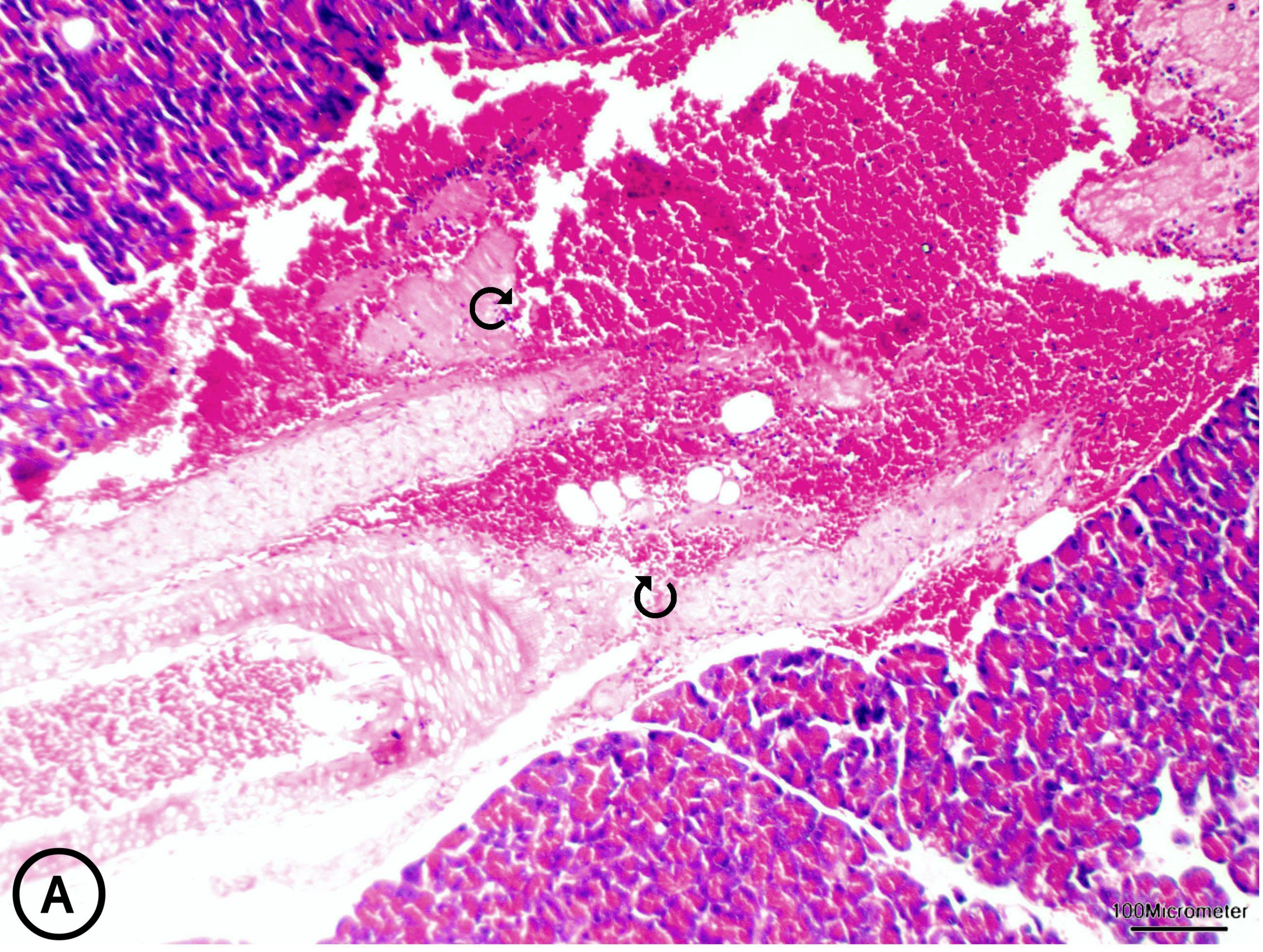
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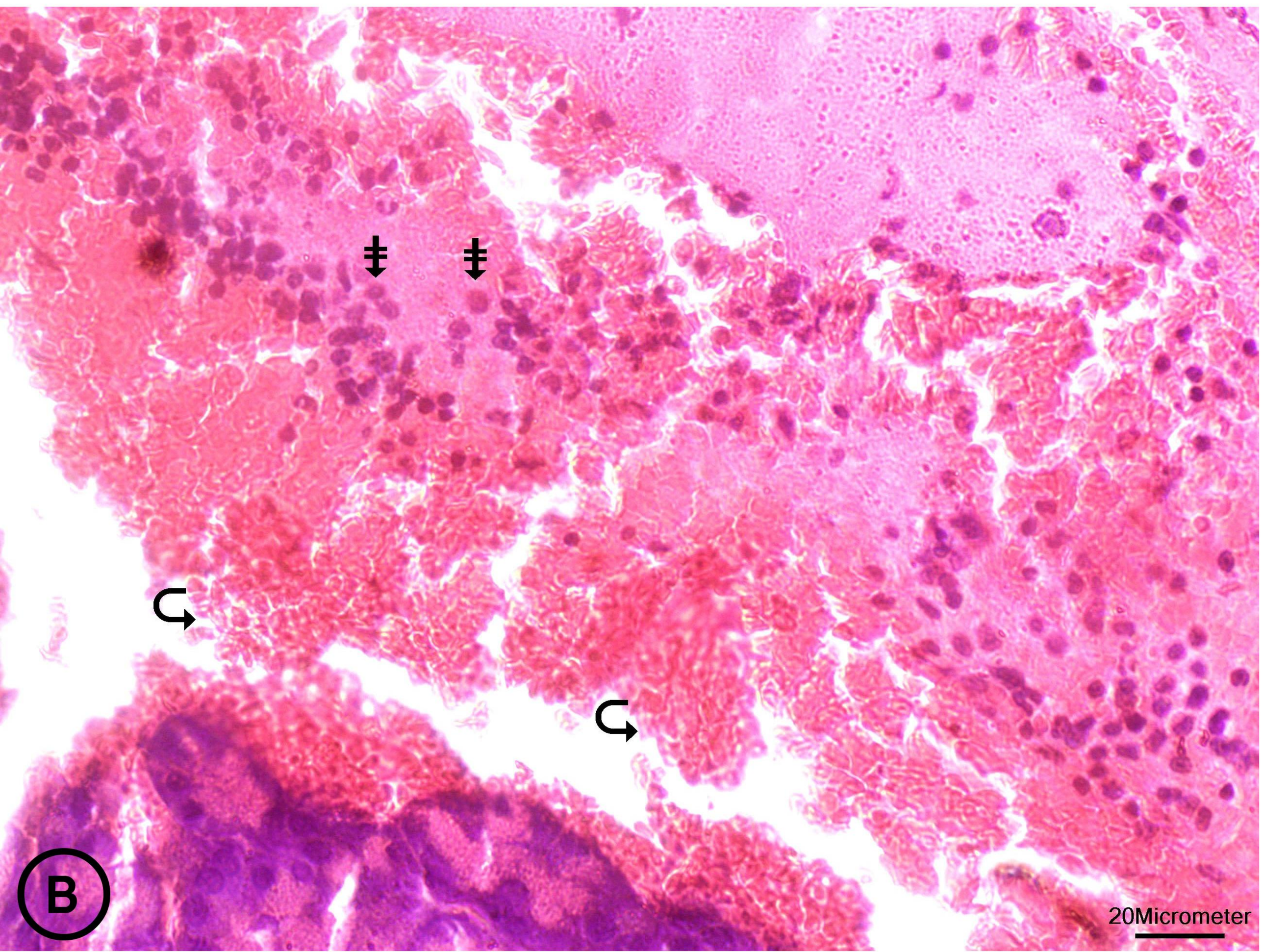
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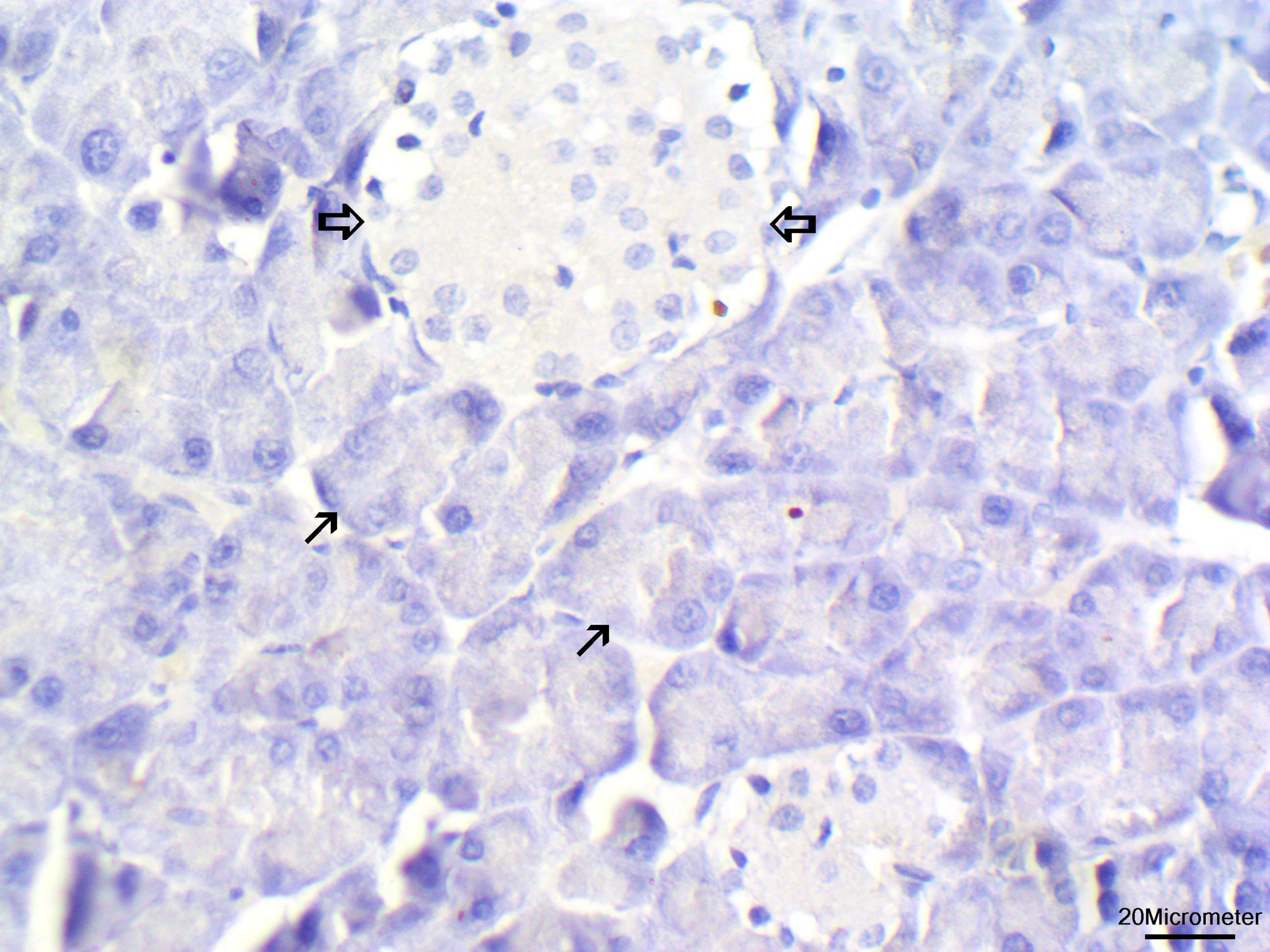
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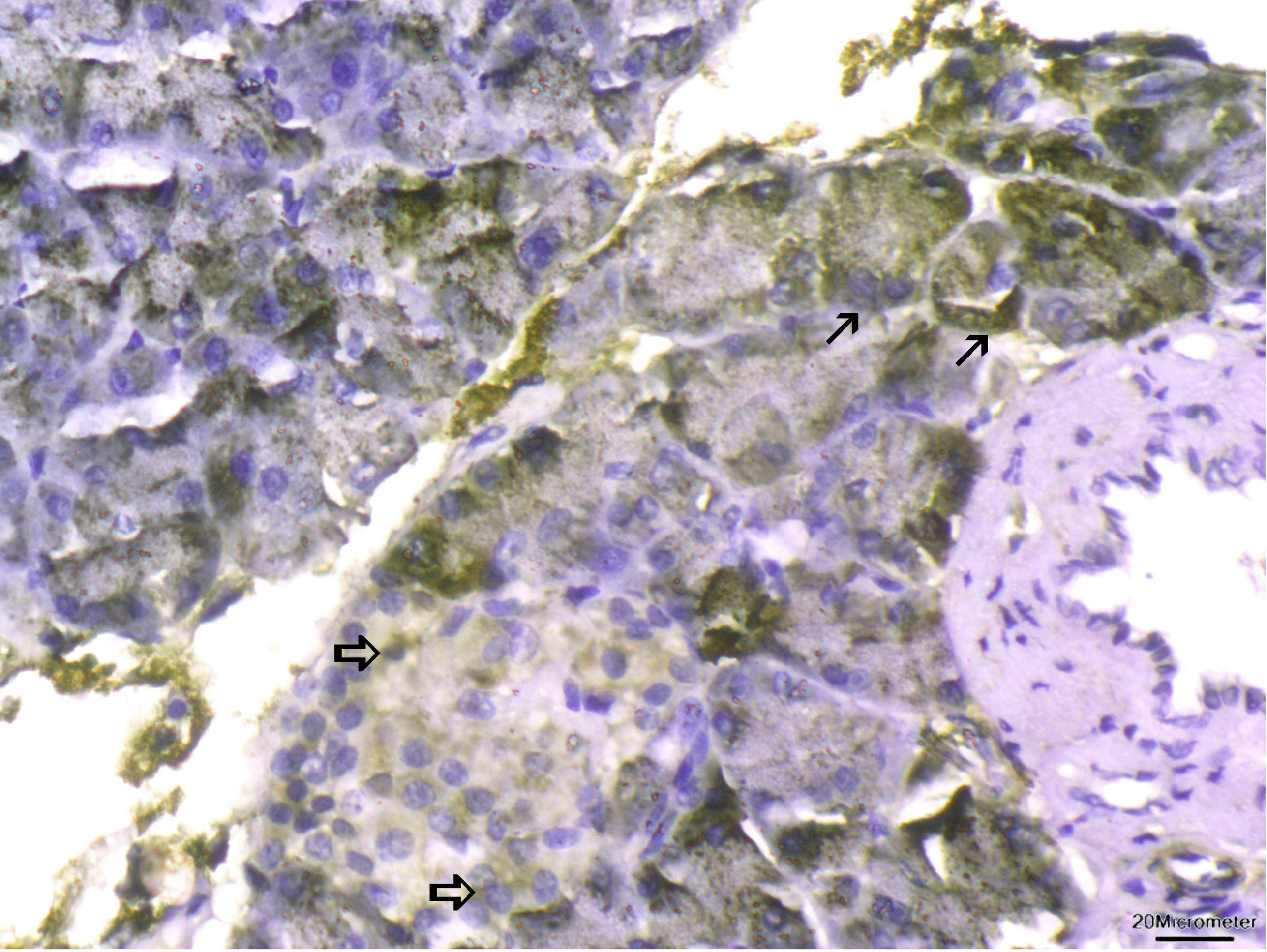
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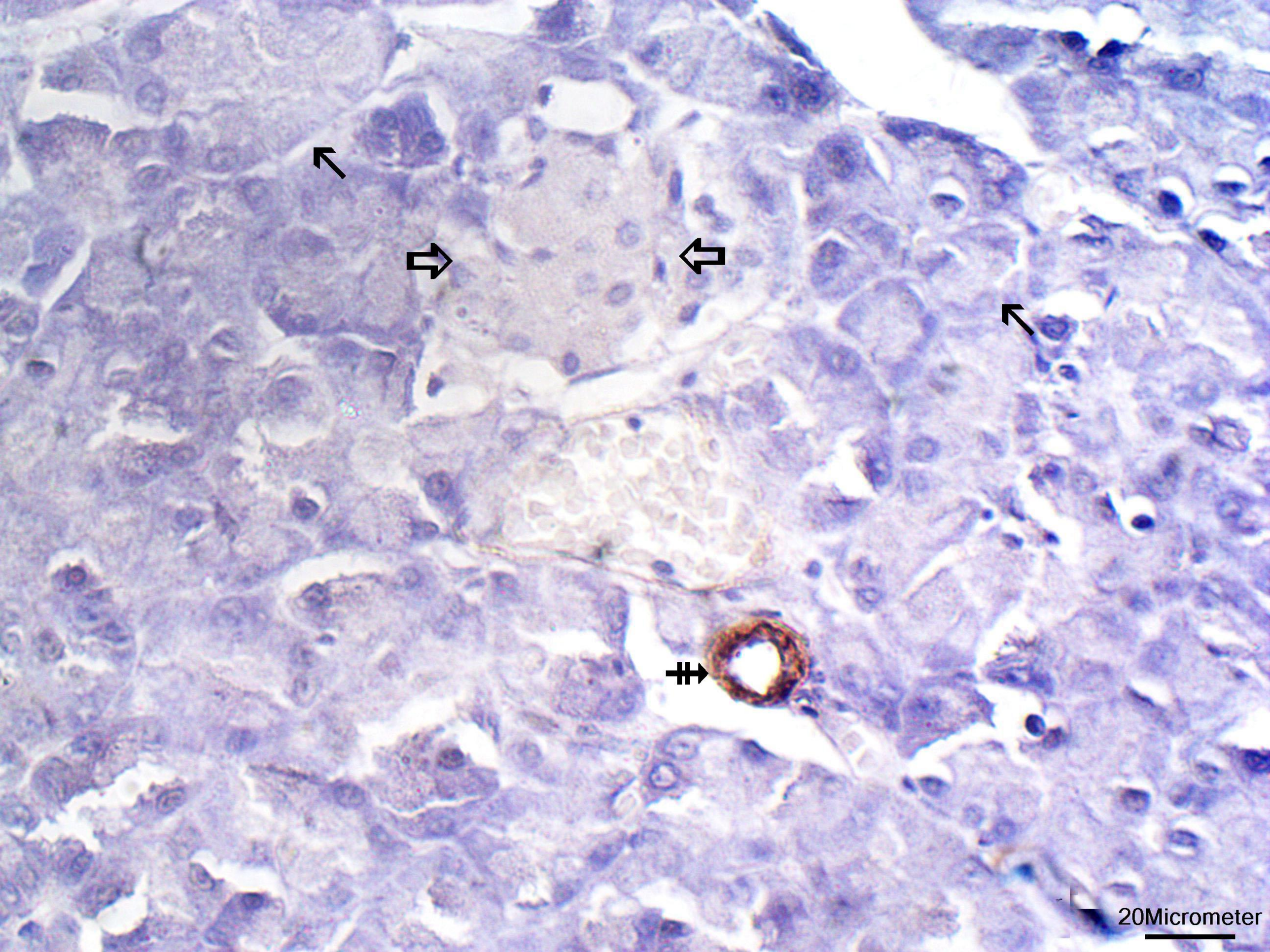
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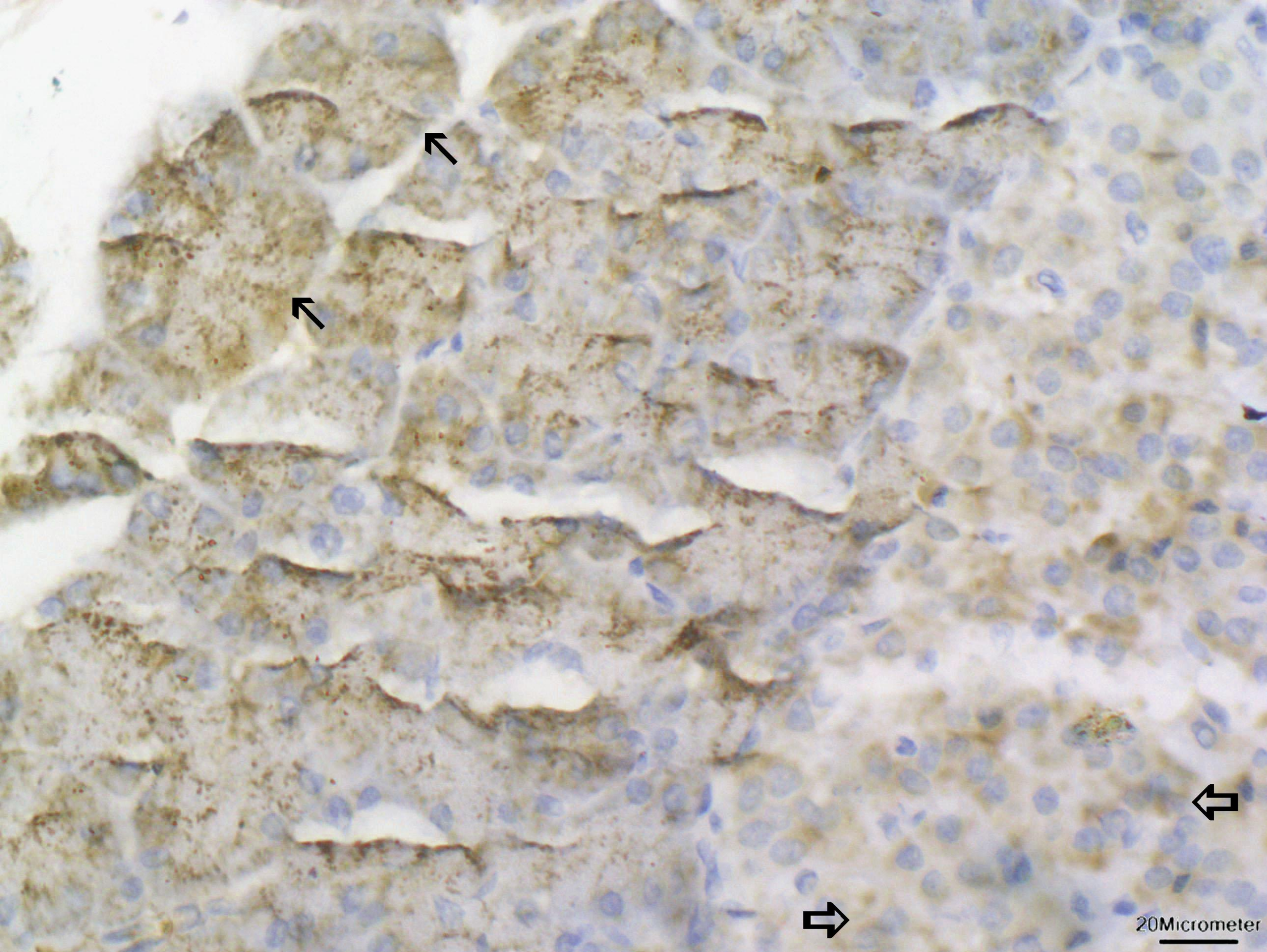
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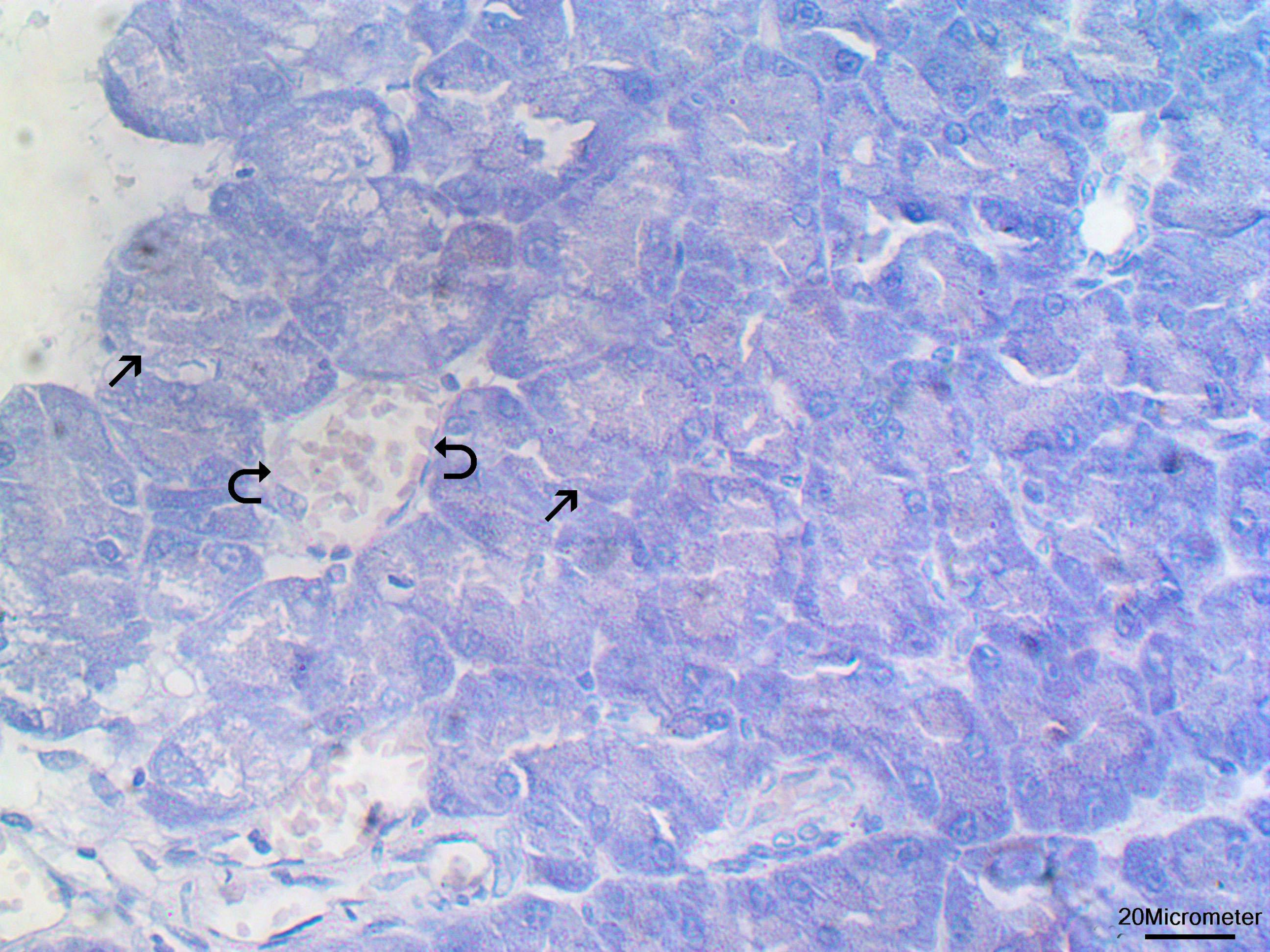
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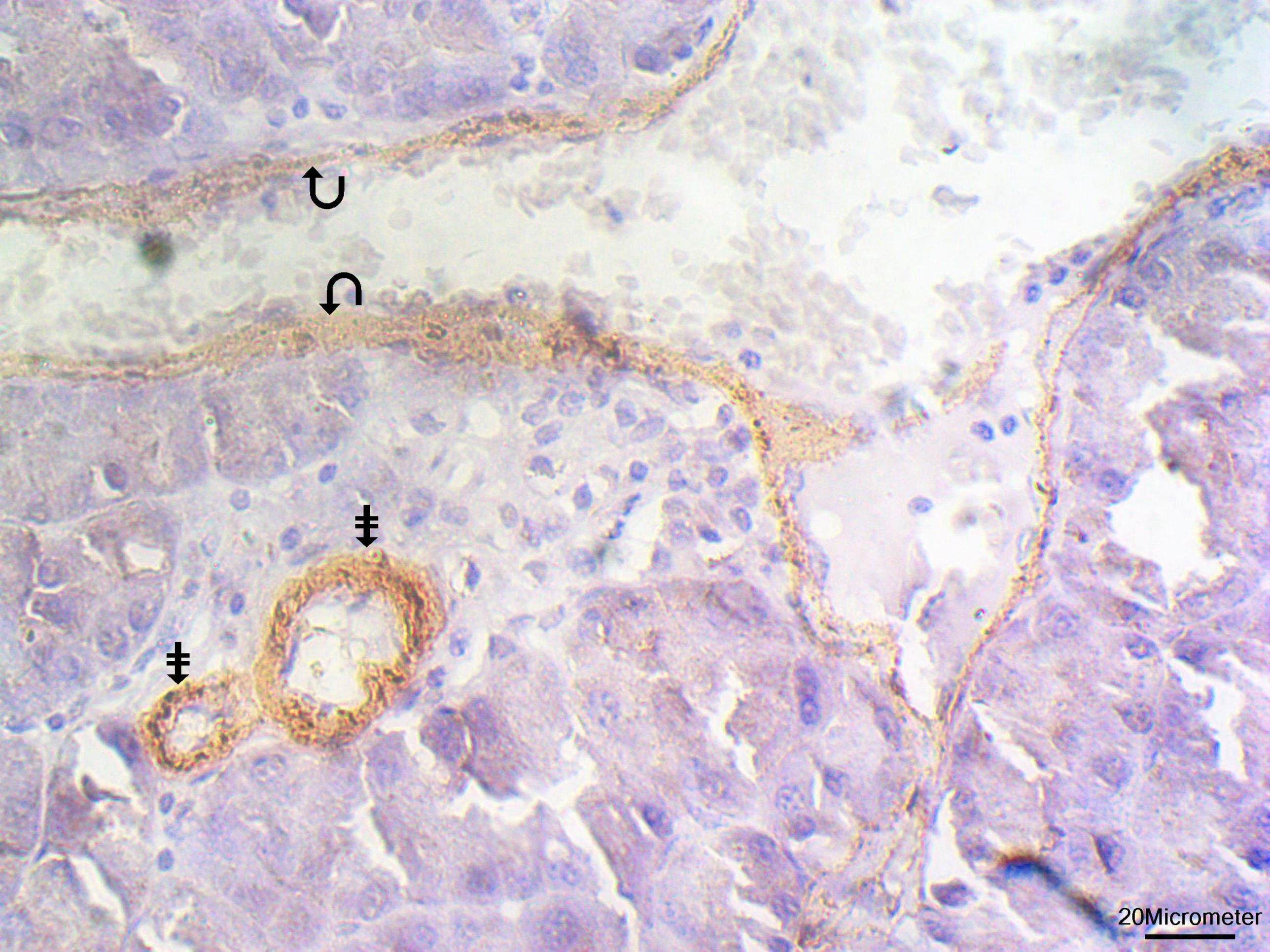
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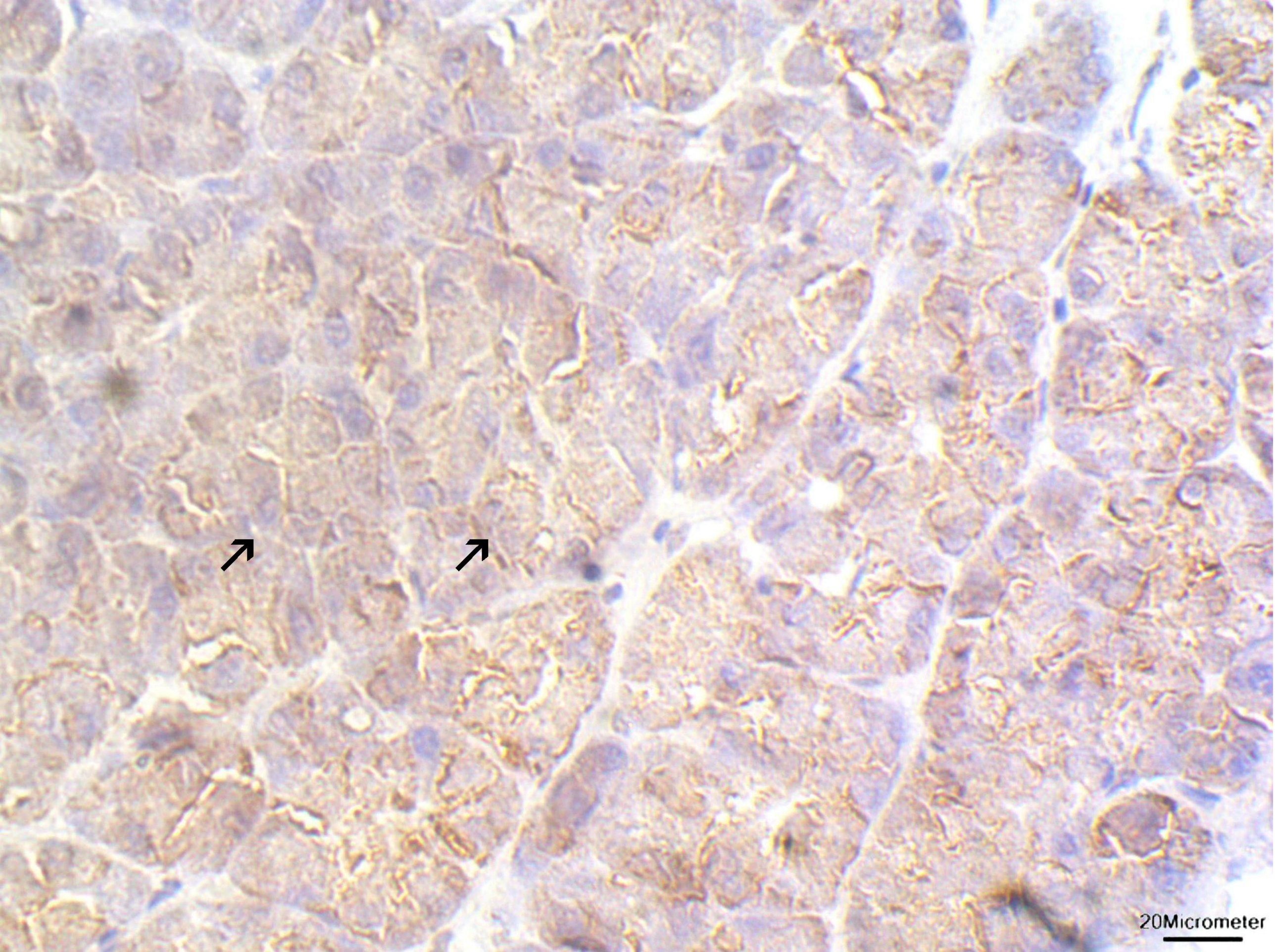
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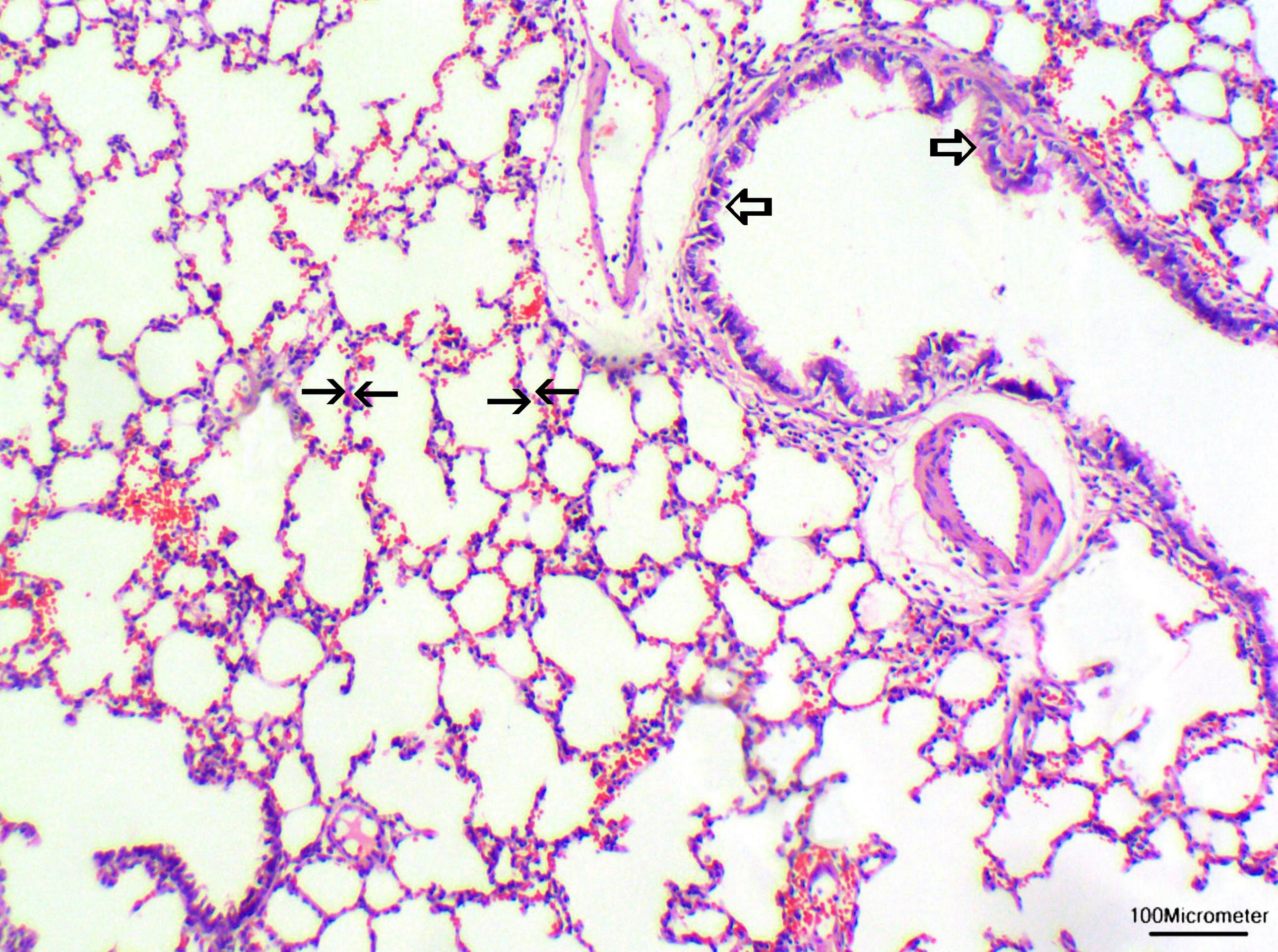
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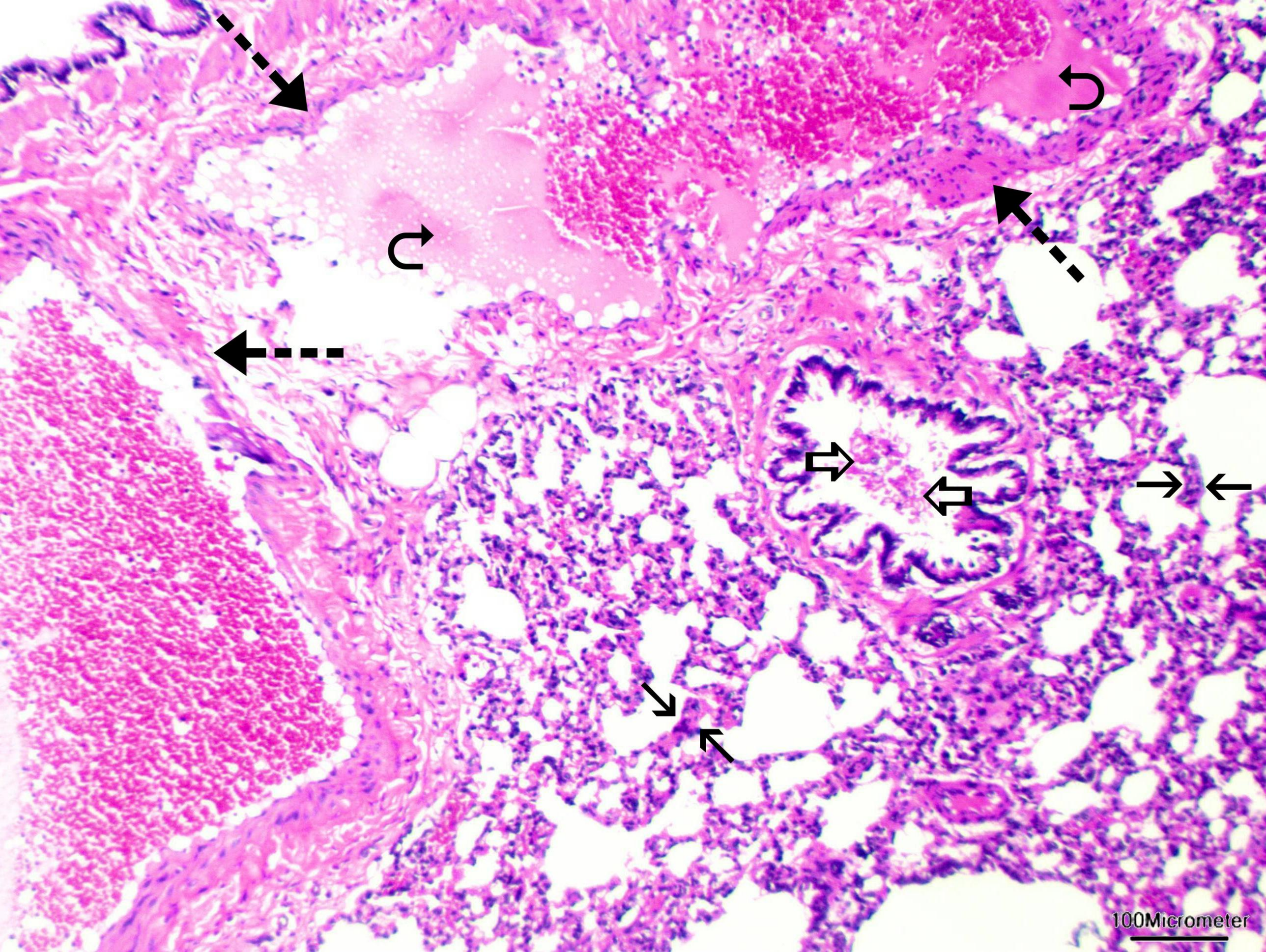
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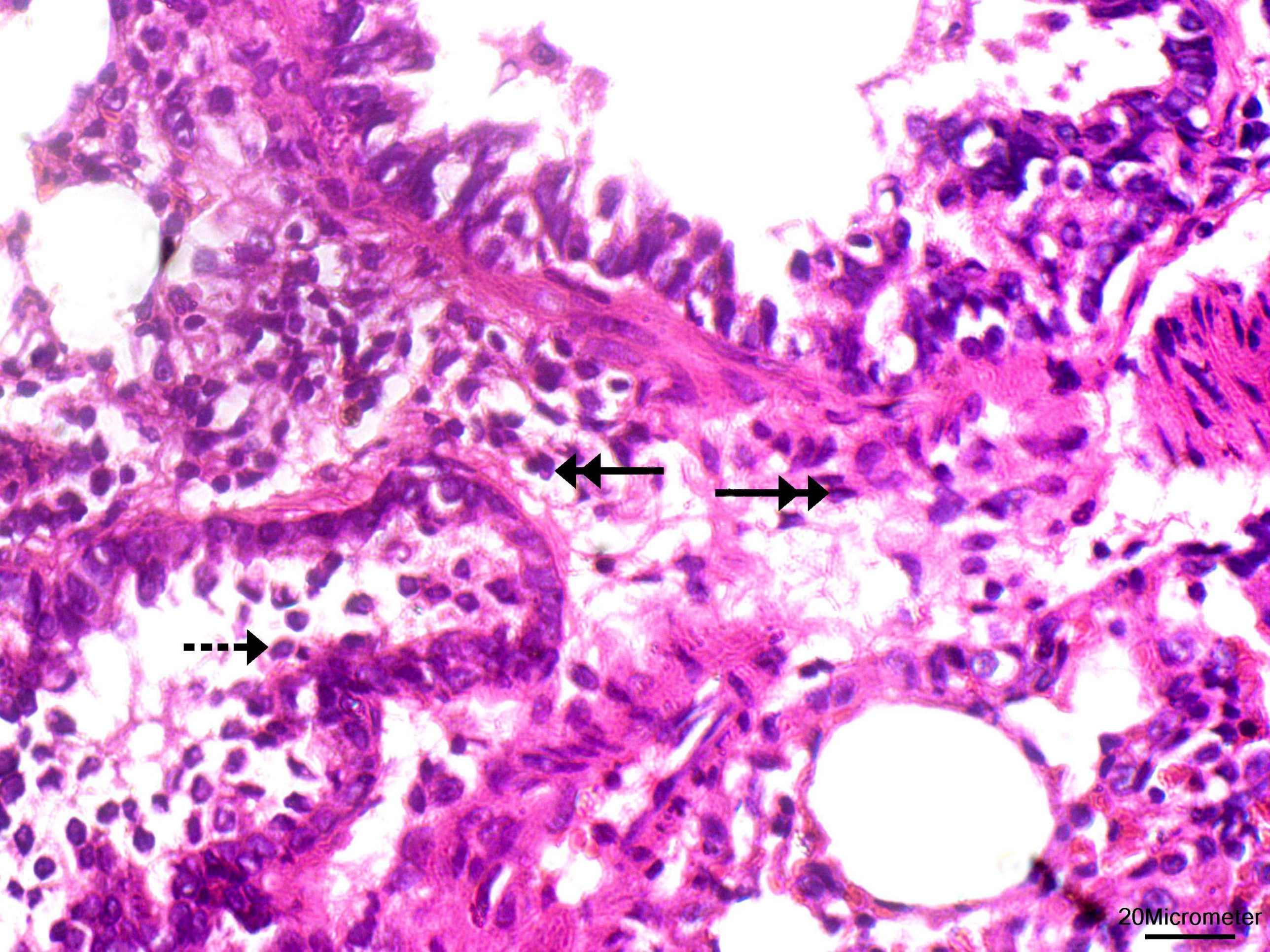
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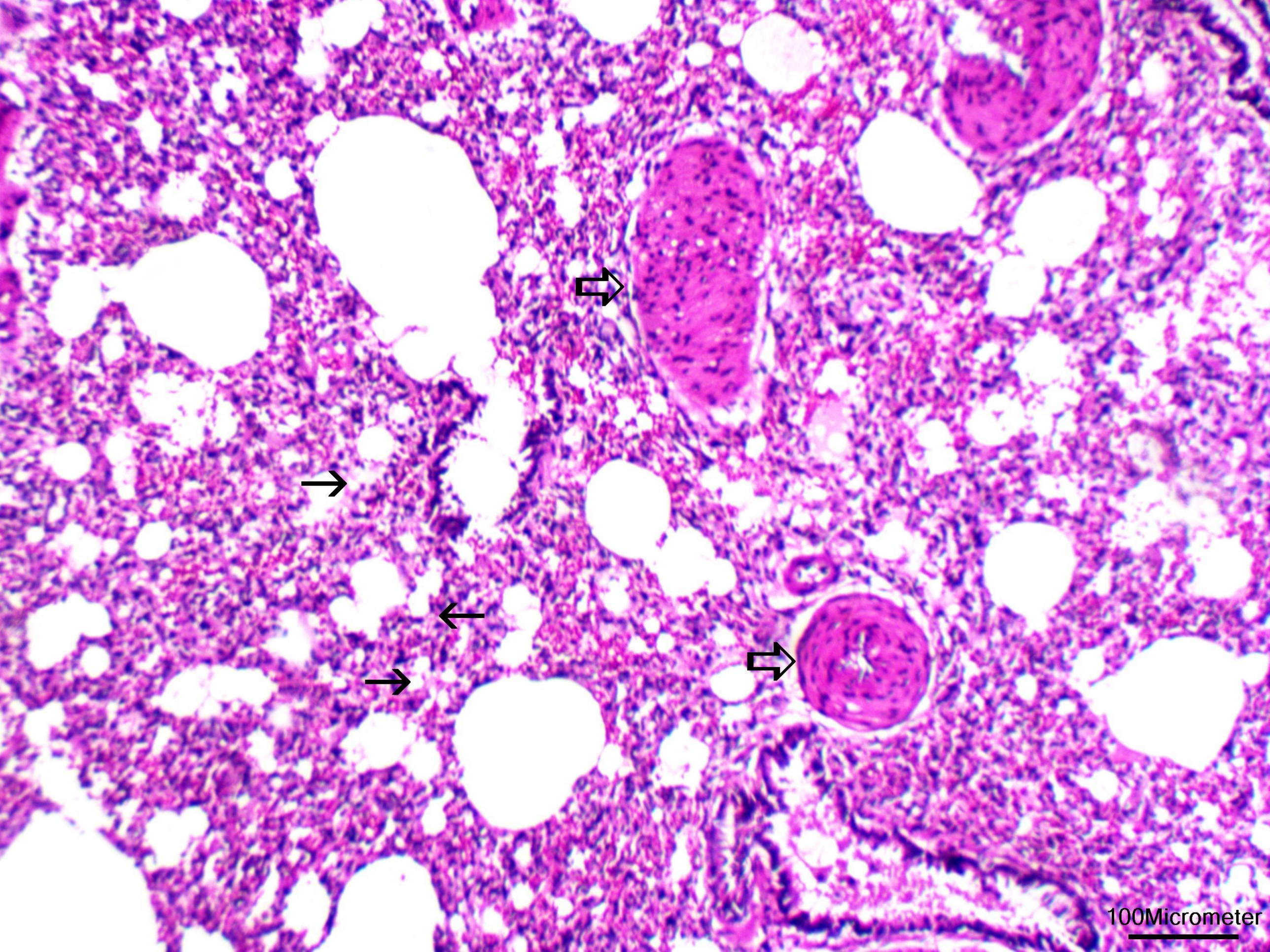
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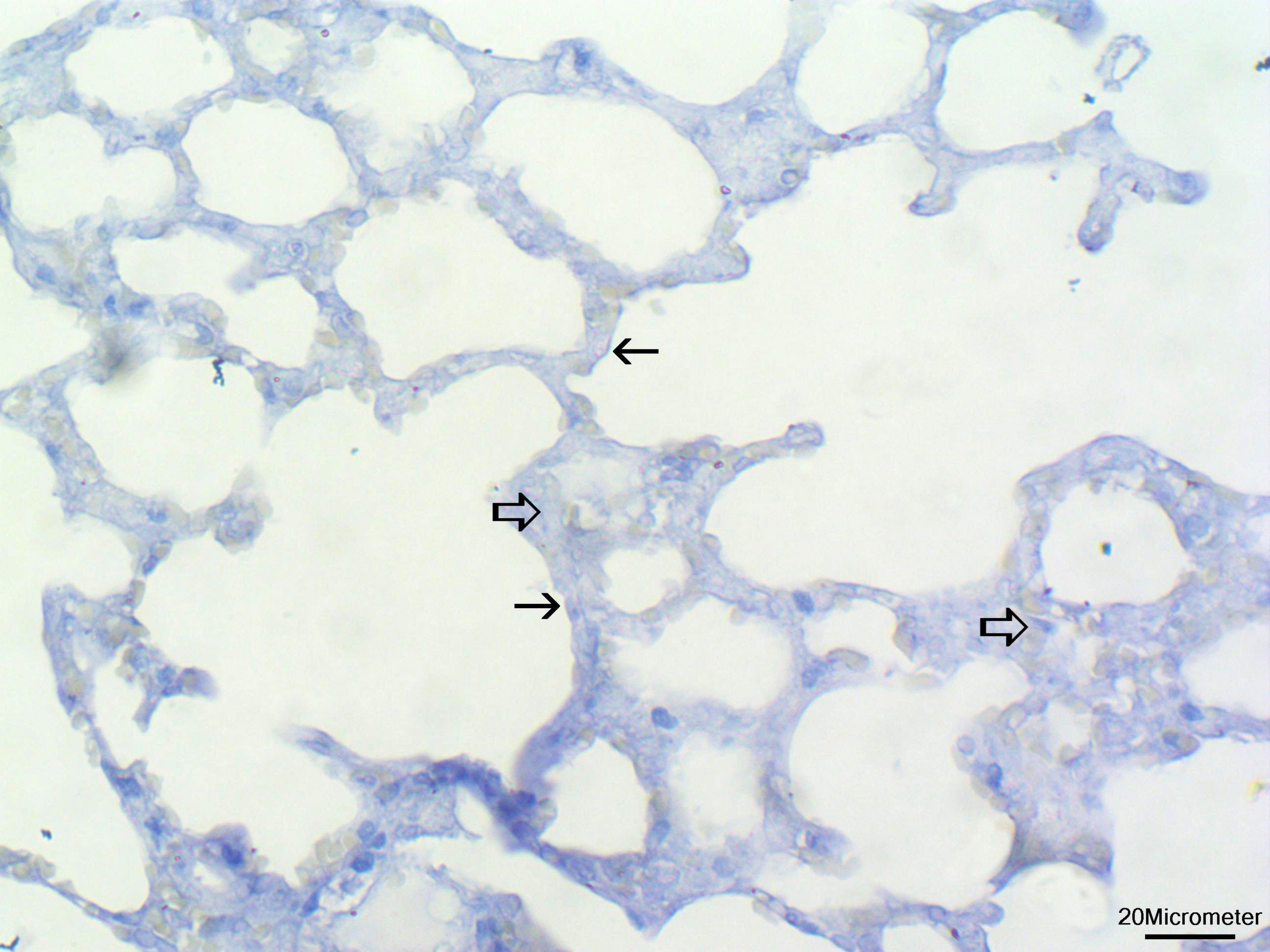
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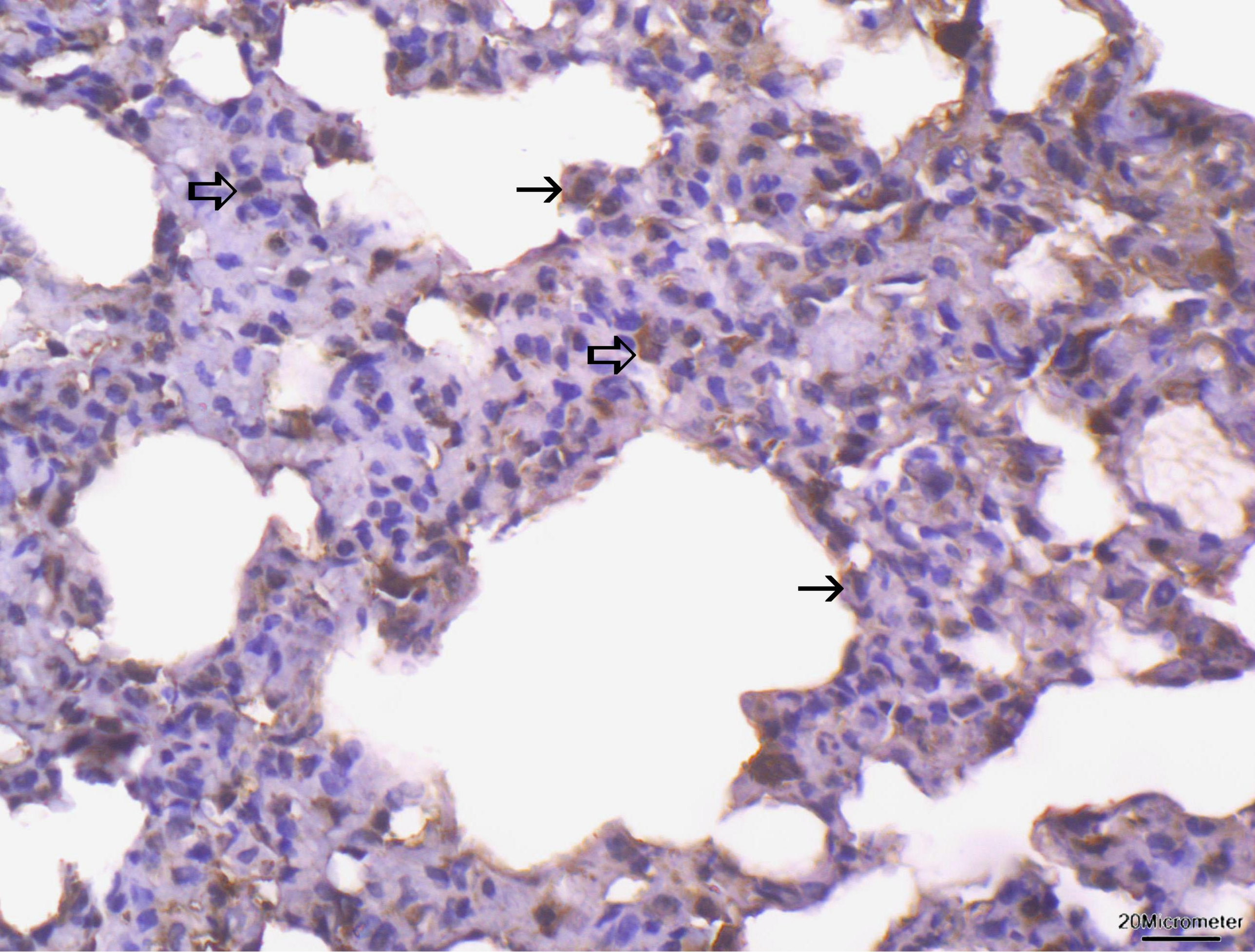
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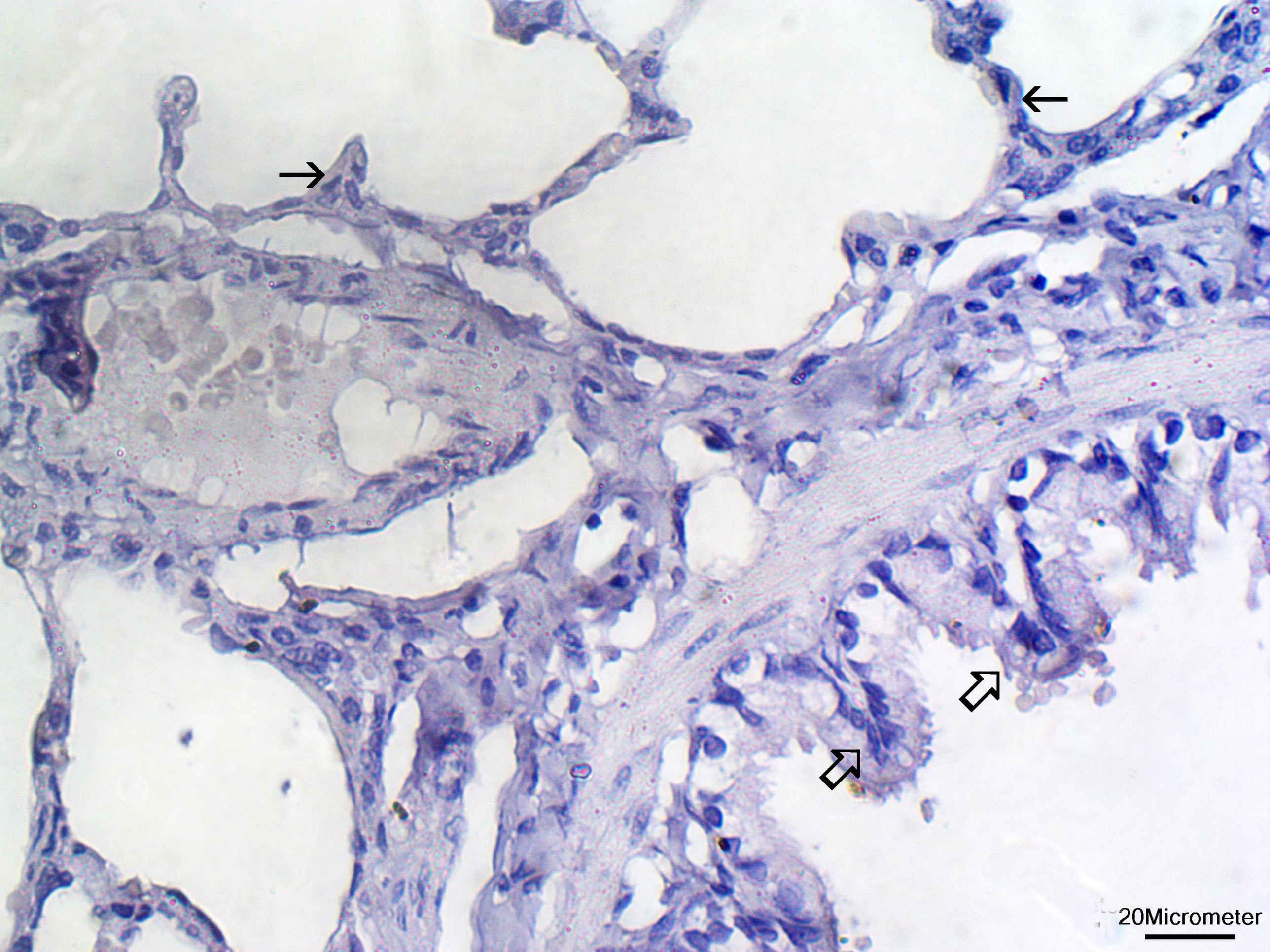
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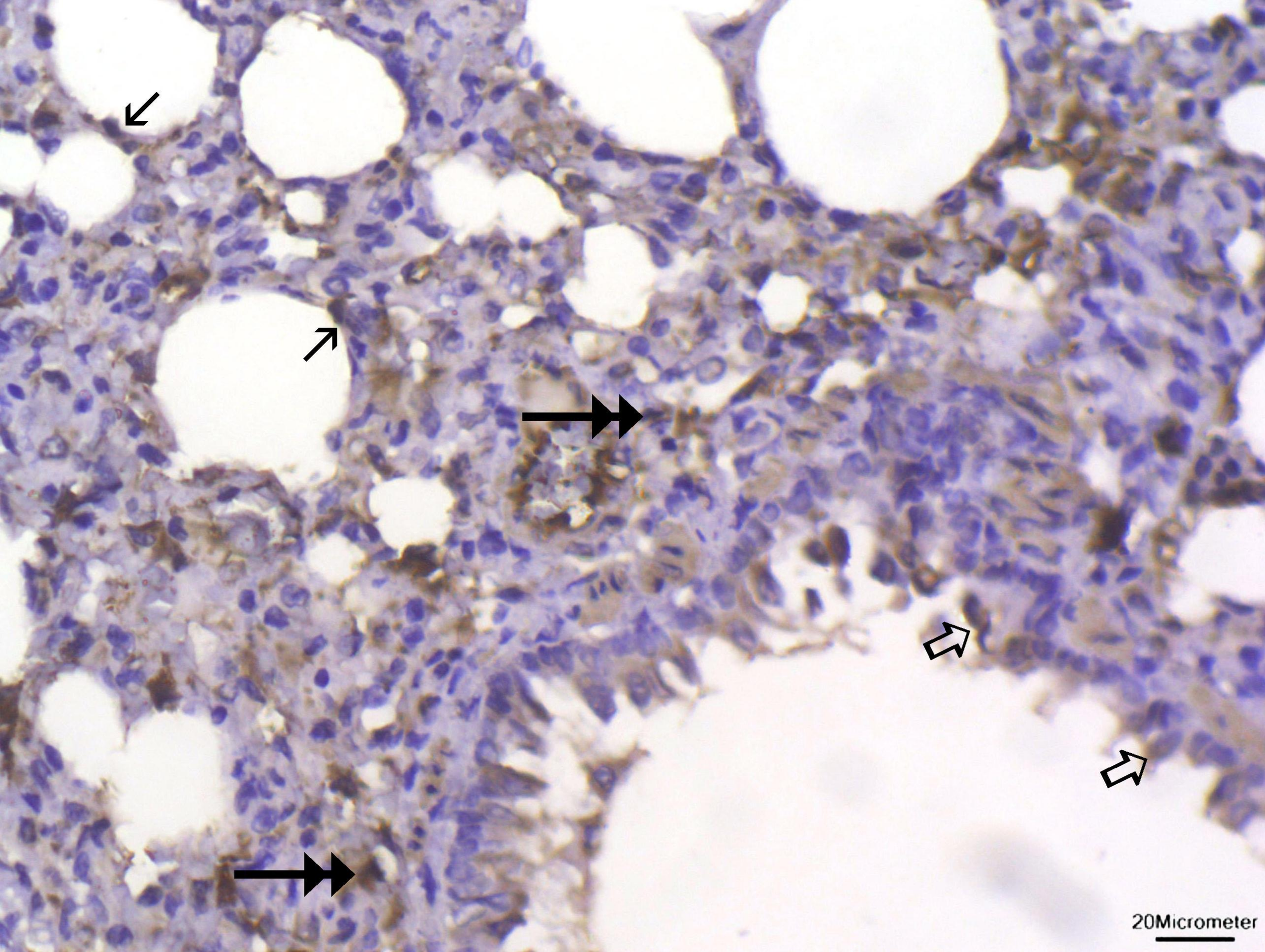
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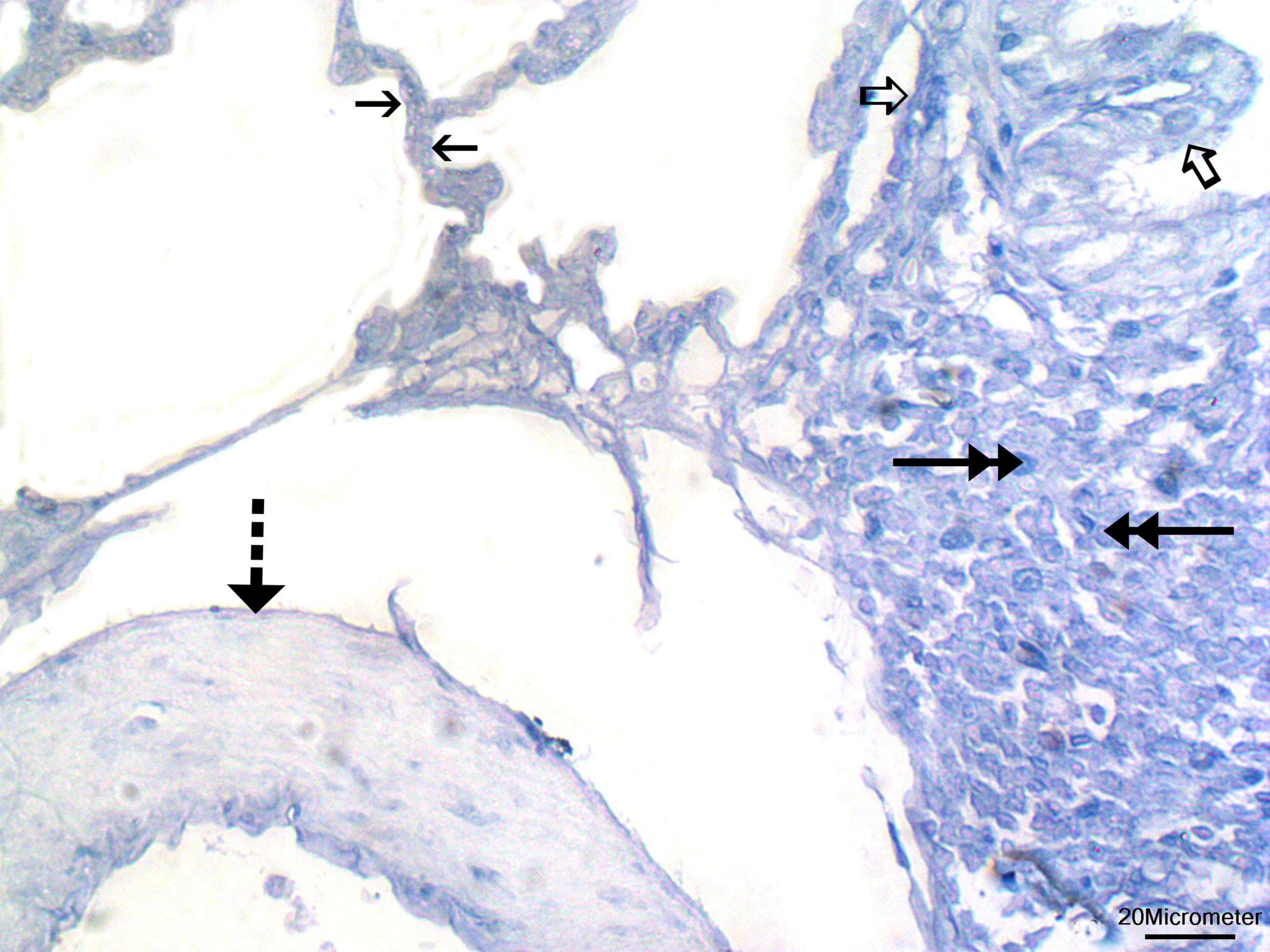
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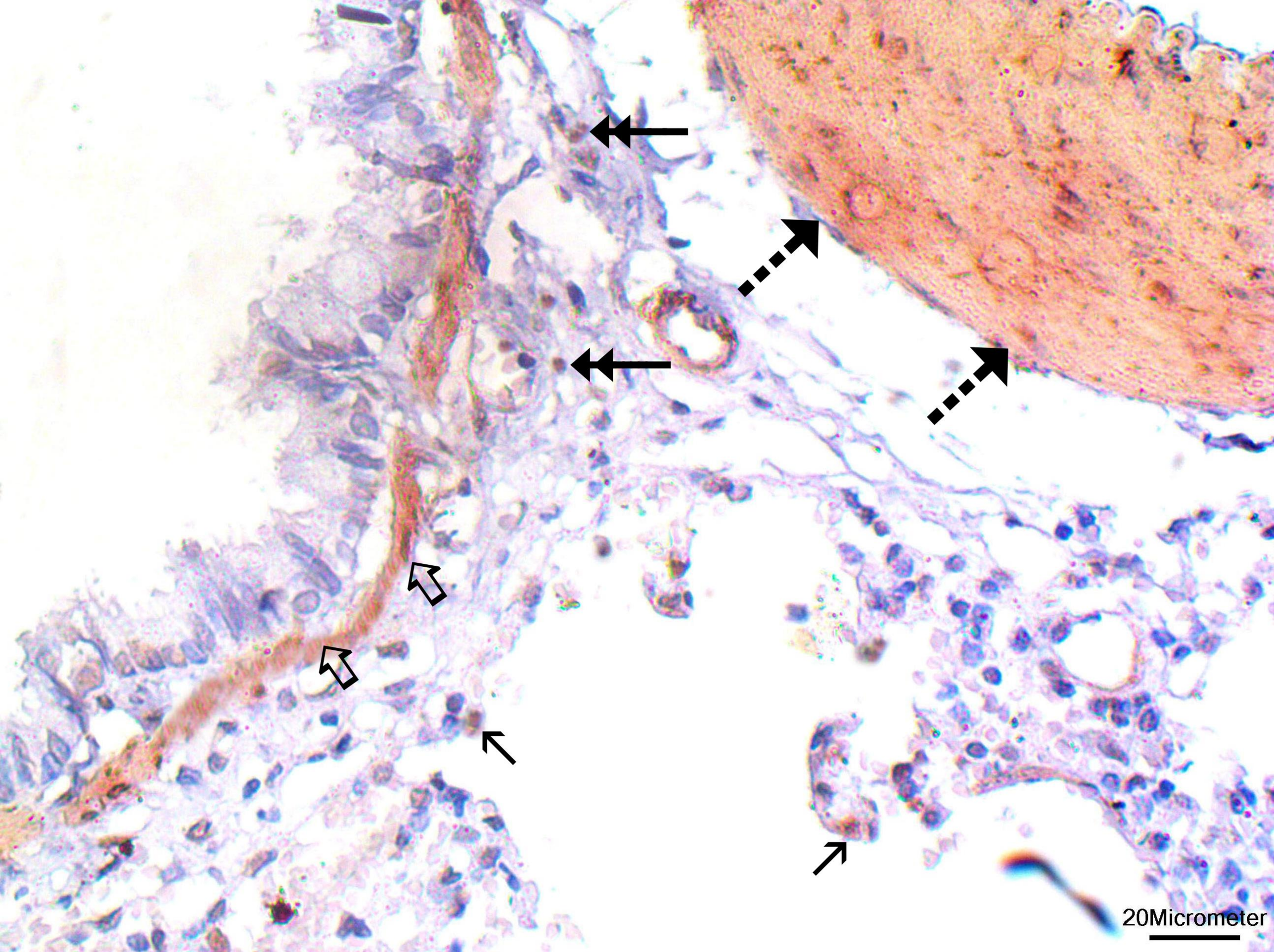
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