



Research Article

Adenomatous lesions of the major duodenal papilla in conjunction with pancreatic heterotopia

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ABSTRACT

Objective: The aim of the research was to study adenomatous and adenomyomatous lesions of the major duodenum papilla with its normal structure and the presence of heterotopic pancreatic tissue in it. **Materials and Method:** The study was carried out on the material of 327 pathoanatomical autopsies taking into account the sex, age, clinical data, pathoanatomical, and clinical diagnoses. The material is divided into two groups: The 1st group - without an ectopic pancreatic tissue in the major duodenum papilla (279 cases) and the 2nd group - with different variants of ectopic pancreatic tissue (48 cases). In each of them, the distribution was carried out according to sex, age, and cause of death. **Results:** Adenomyomatous lesions of the papilla of Vater often combined with pancreatic heterotopia in it - in 23 of 48 cases, various changes were observed in both the papilla wall and ectopic tissue. These include atrophy of the epithelial structures of the papilla, primarily glands, hyperplastic changes in the mucous membrane and glands, significant ductal and cystic transformation, and foci of adenomyosis. **Conclusion:** In the areas of hyperplastic changes in the epithelium of the cystically altered ducts, hyperplasia of stromal elements with a smooth-muscle immunophenotype was determined.

KEY WORDS: Adenoma, Adenomyoma, Papilla of vater, Pancreatic heterotopia

INTRODUCTION

Major duodenal papilla (MDP) is a key anatomical formation in the system of pancreatic and bile outflow and has significant histological and histogenesis features.^[1] In addition to its primary pathology, the problem remains complications of surgical manipulations, which are sometimes no less dangerous than the underlying disease.^[2-4] One of the ways to solve this problem is to take into account as much as possible the structural features of the MDP. It is one of the most difficult factors considered and is the presence of pancreatic heterotopia (ectopia) in it.^[5,6] Morphogenesis of tumor-like changes in MDP is associated with ectopia of pancreatic tissue such as adenoma, adenomyomatous hyperplasia, and cystic lesions have also not been adequately studied.^[7] Tumor-like changes in MDP associated with ectopic pancreatic tissue and its possible subsequent transformation are evaluated in single performed studies, such as

reactive hyperplastic changes or malformations of the papilla, which should be distinguished from its true benign tumors – adenomas.^[8,9] Adenomas of MDP are difficult to diagnose before the appearance of clinically significant complications and symptoms, such as obstruction of the common biliary and pancreatic ducts. Furthermore, adenomas and adenomatous lesions of MDP are often diagnosed after biopsy examination, are precancerous diseases, and can cause diagnostic errors.^[10-12] Adenomas and adenocarcinomas of MDP are most often incidental findings.^[13] In histological examination, adenomas are combined with dysplasia.^[14]

Aim

The aim of the research is to study the morphological features of the MDP in the presence of adenomyomatous, cystic and hyperplastic lesions in norm and heterotopia of the pancreas.

MATERIALS AND METHODS

The study was carried out on the material of 327 autopsies of male and female who died from somatic pathology. The sex, age, pathoanatomical, and clinical diagnoses were taken into account. The collection of

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material for the morphological study was carried out within a period of 4–24 h after death. The common biliary and pancreatic ducts were washed with formalin solution, after which the entire sample was fixed in 10% neutral formalin for 24–48 h, after which the preparation was subjected to standard wiring on a Leica TP 1020 apparatus, paraffinized, 4–5 μm sections were prepared and stained with hematoxylin and eosin using standard protocols and procedures on Leica EG 1150 H, Leica RM 2245, and Leica autostainer XL. To identify the mucus-producing elements, a combined color was used with alcian blue with a PAS-reaction and a pre-stained nucleus with hematoxylin. The immunohistochemical study was performed to identify pancytokeratins (Dako, Cytokeratin, Clone MNF 116), smooth muscle alpha-actin (Dako, Mouse Anti-Human Alpha Smooth Muscle Actin, Clone 1A4), and chromogranin A (Dako). Histological specimens were scanned with Mirax Desk (Carl Zeiss Microimaging GmbH, Germany). Morphometric measurements and statistical computations were carried out using the software panoramic viewer 1.15.4 and Statistica 10.0, respectively.

Main Part

Based on the results of the morphological study, the material is divided into two groups: The 1st group - without ectopia of the pancreatic tissue in the MDP (279 cases) and the 2nd group - with different variants of ectopic pancreatic tissue (48 cases). In each of them, the distribution was carried out according to sex, age, and the nature of the diseases. 250 cases from the total amount of material fell on the second mature and elderly age, which reflects the overall age structure of mortality. The mean age of male and female was 60.7 ± 1.3 and 63.8 ± 1.2 years, respectively.

Macroscopically external changes in the MDP, characteristic of adenomyomatous lesions of MDP, were not detected. The well-expressed folds of the mucous membrane were observed in 47.9%, slightly expressed in 27.2%, there was no formed relief of the mucous membrane of the papilla in 14.2% of cases.

At microscopic examination in the same group in 10.7% polypous changes of folds-valves of a papilla in the form of a sharp thickening due to stroma and hyperplasia of epithelium of the free ends, protruding in a lumen of the aperture of a papilla is found out.

The own glands of the papilla wall were characterized by a relatively compact arrangement of rounded mucous end sections with a diameter of 50–60 μm . The mukocytes had a high prismatic shape; the mucous secret contained both neutral periodic acid Schiff-positive mucins and acidic alcyanophilic mucins. The content of mixed and alcianophilic secretion in the apical cytoplasm was also characteristic of the protocol structures in the papilla wall. The glands of

the wall of the common biliary and pancreatic ducts were disposed in a fragmented, non-uniform in size, often irregularly rounded; neutral mucins predominated in their secretion. In addition, the glands of the MDP wall were located both in the thickness of its mucous membrane and were introduced into the thickness of the sphincters, forming there a glandular-muscular layer.

Histologically, strata consisted of interlayers of collagen-new fibers and the absence of elastic elements, the cellular composition represented by spindle-shaped fibroblast-like elements with a scant amount of lymphoid cells. In a number of observations in the MDP, only small, or almost exclusively, small ductal structures forming into lobules, as well as single acini or individual small groups of acinar cells, not formed into typical secretory sections of pancreatic tissue, were detected. In this case, the flow structures had a diameter of 12–40 μm , were characterized by a compact arrangement, and were formed by a single-layered low prismatic or cubic epithelium with a clearly detectable secretion of mixed (cyanophilic and periodic acid Schiff-positive) mucins. Such changes were detected in 8 cases in combination with a pancreatic heterotopy. In all cases, the cluster centers of small ducts in the MDP were multiple, ranging in size from 100 to 350 μm . The stroma between the protocol structures had a fine-fibrous structure, a moderately dense cellular composition represented by lymphocytic-type elements, spindle-shaped cells with a sparse cytoplasm, dense, elongated nuclei with pointed ends that resemble fibrotic-type elements, in part with myoepitheliocytes. In places, there was an external similarity with the structure of the non-lactating mammary gland due to a multitude of small ductal structures. The immunohistochemical study revealed fusiform cells with a smooth-muscle immunophenotype. In general, a picture is formed of the formations characterized as adenomyomatous

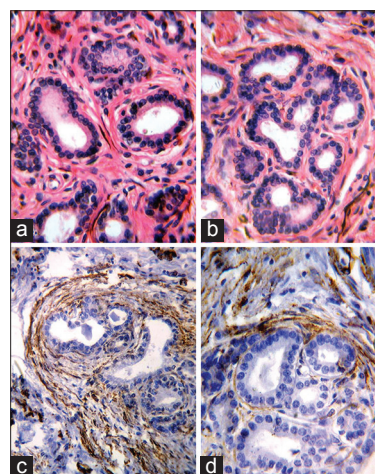


Figure 1: Adenomyomatous lesions of the papilla of Vater. (a and b) Hematoxylin and eosin, (c and d) smooth muscle actin, clone 1A4 + LSAB kit, DAB; “Dako”; $\times 320$

Table 1: Frequency of MDP changes in some diseases of the digestive system

MDP changes	Diseases of the digestive system					Without lesions	Total
	Cirrhosis	Hepatitis	Gastric ulcer	Pancreatitis	Cholecystitis		
Structural elements atrophy of papilla of Vater	3	1	2	6	4	7	23
Structural elements hyperplasia of papilla of Vater	1	3	1	2	2	14	23
Adenomyosis	2	2	3	1	1	8	17

MDP: Major duodenal papilla

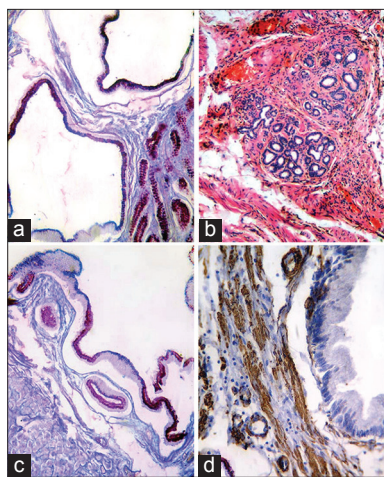


Figure 2: Cystic transformation and sclerosis of the papilla of Vater. (a and c) Alcyan blue + PAS - reaction staining, (b) Hematoxylin and eosin staining, (a and b) $\times 72$, and (d) smooth muscle actin, clone 1A4 + LSAB kit, DAB; “Dako”; (c and d) $\times 320$

(muscular-ferruginous and myoepithelial) hamartoma or adenomyoma [Figure 1].

Atrophy of the epithelial structures of the papilla (glands, hyperplastic changes in the mucous membrane and glands, pronounced ductal and cystic transformation of the ectopic tissue, and foci of adenomyosis) was revealed in 23 (47.91%) observations in combination with pancreatic heterotopia. In the group without pancreatic ectopy, similar changes were detected in 63 cases (22.58%).

At pancreonecrosis and chronic pancreatitis, cholelithiasis, the atrophy of the glands of the papilla was more frequent. Hyperplasia of its epithelial structures and adenomyosis was observed in the sample we studied and outside of the connection with these diseases, which may indicate their primacy as tumor-like and benign tumoral changes [Table 1].

Statistical analysis confirmed the relationship of atrophic changes in the bronchial asthma gland with cholelithiasis and pancreatitis ($\chi^2 = 4.512$ and 10.857 , respectively).

However, the above assessment of various changes in the papilla is conditional, since their combinations

are accounted for by the predominant type. In particular, the atrophy of the MDP glands in the presence of fibrotic changes in its wall in 6 cases out of 16 was mosaic in nature and was combined with foci of hyperplasia of the superficial epithelium and glands, and in 3 cases it was combined with foci of adenomyosis. Hyperplastic changes in one-third of cases were combined with adenomyosis.

We identified adenomyosis in the presence of foci of pronounced glandular hyperplasia and muscle elements in the type of nodes that go beyond the sphincter area of the papilla and the muscular-ferruginous layer, with the vortex-like orientation of the smooth myocyte bundles, random for the muscle structures of the MDP, chaotic arrangement and gland polymorphism [Figure 1].

The ductal structures in the foci of fibrosis have different diameter along with small protocoietic formations; there are enlarged deformed ducts with a star and branching shape of lumens, epithelial polymorphism and the presence of foci of pseudostratification and squamous cell metaplasia. In the thickness of the mucosa and the musculo-glandular layer of the papilla wall, small ductal formations along with annular fibrous structures formed delimited nodes, which under the small increase are of the form “fibroaden” [Figure 2b].

In the structure of their stroma, collagen fibers and fibrocyte elements predominated. When combined atrophic-sclerotic changes of the papilla with foci of adenomyosis such nodes went beyond the sphincter of the papilla. Significant changes in the glands of the papilla and pancreatic heterotopia were the cystic transformation of the ducts, in which both sclerotic changes in the papilla wall and hyperplasia of its epithelial structures [Figure 2a and b] were observed. The diameter of the cystic cavities reached 0.1 cm. The epithelial lining was characterized by uneven thickness of the epithelium with the presence of areas of its flattening and hyperplasia with pseudostratification. Around cysts, there was a clearly delimited layer of fibrous tissue. The color of mucus in the epithelium of the cysts revealed foci of hypersecretion, combined with its sharp decrease or absence, with the appearance of production sites only of neutral mucins

or exceptionally acidic alcianophilic, not typical of the protocol structures of the MDP and the pancreas in the norm [Figure 2a and c]. In the areas of hyperplastic changes in the epithelium of the cystically altered ducts in the form of micropapillary growths and pseudotrification, hyperplasia of stromal elements with a smooth-muscle immunophenotype [Figure 2d] was determined.

CONCLUSION

1. Hyperplastic, atrophic, sclerotic, and cystic changes in MDP were detected at a frequency of 22.58% and 47.91% in the group without pancreatic ectopia and in combination with it, respectively.
2. Hyperplastic, atrophic, sclerotic, and cystic changes of MDP reliably more often are combined with diseases of the gastrointestinal tract.
3. A large number of elements with a smooth-muscle immunophenotype are located around the adenoma.
4. In the epithelium of MDP at atrophic-sclerotic processes, both qualitative and quantitative changes in mucus secretion are observed.

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