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Abstracts

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Aims and Scope

Mission statement: To advance the scientific basis of human pathology by the publication (encouragement and dissemination) of high quality research (including molecular and translational studies) and thereby contribute to patient care. Manuscripts of original studies reinforcing the evidence base of modern diagnostic pathology, using immunocytochemical, molecular and ultrastructural techniques, will be welcomed. In addition, papers on critical evaluation of diagnostic criteria but also broadsheets and guidelines with a solid evidence base will be considered. Consideration will also be given to reports of work in other fields relevant to the understanding of human pathology as well as manuscripts on the application of new methods and techniques in pathology. Submission of purely experimental articles is discouraged but manuscripts on experimental work applicable to diagnostic pathology are welcomed. Biomarker studies are welcomed but need to abide by strict rules (e.g. REMARK) of adequate sample size and relevant

marker choice. Single marker studies on limited patient series without validated application will as a rule not be considered. Case reports will only be considered when they provide substantial new information with an impact on understanding disease or diagnostic practice.

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Method: 61-year-old patient complained on the exertional dyspnea and was admitted to the clinic. Lower extremity edema, decreasing exercise tolerance appeared 3 years ago. History of hypertension and aortic stenosis made it difficult to carry out differential diagnosis of accumulation disease. Patient underwent echocardiography, single-photon emission computed tomography (SPECT) with ^{99m}Tc -PYP, endomyocardial biopsy and genetic analysis. We used Congo red staining, polarization and immunohistochemistry.

Results: Transthoracic echocardiogram revealed restrictive diastolic dysfunction of both ventricles. Ejection fraction (30 %) and global longitudinal strain (2–3 %) were reduced. SPECT showed the high accumulation level of ^{99m}Tc -PYP in the myocardium of left and right ventricles. The heart-to-contralateral ratio was 2,66. The amyloid deposits were located in myocardial interstitium as well as in the wall of small vessels. Immunohistochemical analysis revealed the expression of transthyretin in the areas of amyloid deposition. Genetic research was done by Sanger's sequencing method. The replacement Phe53Leu in the TTR gene was found and concluded as hereditary ATTR.

Conclusion: ^{99m}Tc -labeled pyrophosphate scintigraphy is an effective non-invasive diagnostic method that allows to identify cardiac ATTR.

PS-12-008

Morrow's myectomy

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Objective: Septal sub-aortic myectomy, invented by Andrew Glenn Morrow, was first used to treat left ventricle outflow-tract obstruction in Hypertrophic Cardiomyopathy and afterwards extended to other prominent ventricular hypertrophies and septal angulation. The authors intend to present the histomorphological pattern of a series.

Method: Retrospective study of patients submitted to surgical septal sub-aortic myectomy (June 2007-July 2016), due to septal hypertrophy. Demographic, clinical, echocardiographic and anatomo-pathological data was evaluated.

Results: 56 patients, 37 (66.1 %) females, median age = 67.5 year-old, 26 (46.4 %) due to calcified degenerative aortic valve, 25 (44.6 %) with hypertension history, 30 (55.6 %) due to symptomatic isolated obstructive septal hypertrophy. According to clinical and echocardiographic criteria, 25 patients (44.6 %) had obstructive hypertrophic cardiomyopathy phenotype. All patients with aortic valvular stenosis were submitted to prothesis implantation and myectomy, 12 patients (21.4 %) to isolated myectomy and the other (32.2 %) to myectomy and a mitral valve apparatus surgical procedure. The final anatomo-pathological diagnosis was hypertrophy in 52 cases (92.9 %), aortic sub-valvular membrane (stenosis) in 2 (3.6 %) and hypertrophic cardiomyopathy in 2 (3.6 %).

Conclusion: Morrow's Myectomy relevance relies on the diagnosis, with anatomo-pathological characterization of surgical specimens' microscopic features, as well as on patients' daily life improvement and prevention of many sudden cardiac deaths.

PS-12-009

Cardiac Myxoma: Review of clinical and histopathological features of 8 cases at Hospitalary Complex of Navarra

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Objective: Myxoma is the most common primary tumour of heart, although still rare. These tumour are benign but malignant in a sense that often embolizes and may cause severe complications. We report our experience with cardiac myxoma in adults at Hospitalary Complex of Navarra.

Method: Eight patients resected for primary cardiac tumours between Jan. 2007 and Jan 2017. We retrospectively reviewed their clinical, immunohistochemical and pathological findings.

Results: The mean age at the time of resection was 50.37 years (range 21–73). All the patients were females and one case was diagnosed during pregnancy. The most common clinical presentation was arterial embolisms (80 %). Most common location was left atrium. Mean size were 24.85 mm. Multiple myxomas were found in two out of eight patients reviewed and both tumour had recurrence 2 years after resection. All the tumours had characteristic stellate cells in a myxoid background, and 25 % showed ossification, 37.5 % Extramedullary haematopoiesis, glandular structures (12,5 %) and granulomas (12,5 %). All cases revealed strongly positive vimentin and CD34.

Conclusion: Cardiac myxoma is more common in young women. Although cardiac myxoma is a benign tumour, embolisms may cause severe complications. A better understanding of the histopathologic features of cardiac myxomas would facilitate the proper management and improve prognosis.

PS-12-011

Lack of expression of ascending aortic wall estrogen receptor beta - a potential clue for aortic valve stenosis?

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Objective: Aortic valve stenosis may be associated with post-stenotic dilatation of the stiff-walled atherosclerotic ascending aorta, which is seldom at risk for dissection. Aortic wall estrogen receptor beta (ER) positivity may protect from atherosclerosis of the dilated ascending aorta. We studied the presence of aortic valve stenosis during dilatation of the ascending aorta in respect to aortic wall ER positivity.

Method: Aortic wall histology (Elastase, HE, AbPAS staining) and immunohistochemistry for ER, T/ B-lymphocytes, plasma cells, macrophages, endothelial cells, smooth muscle cells, and cell proliferation, were performed in 30 patients that underwent surgery for the ascending aorta, and the samples were grouped according to presence of ER positivity.

Results: 23 patients were operated due to dilated ascending aorta and 7 due to dissection. Two patients with ER had aortic valve stenosis, in contrast to eight without ER. Macrophages of the media were increased in patients with ER as compared to those without ER (1.75 ± 0.28 vs 1.08 ± 0.17 , $p = 0.044$, respectively). Receiver operating characteristic curve (ROC) analysis showed that dilated ascending aorta with medial ER is seldom associated with aortic valve stenosis (AUC 0.805; SE 0.081; $p = 0.008$; 95 % CI 0.646–0.964). Aortic wall medial ER is inversely correlated with the severity of aortic valve stenosis (R2 linear = 0.937, $p = 0.009$).

Conclusion: Lack of dilated ascending aortic wall ER is associated with aortic valve stenosis reflecting atherosclerosis and stiffness of the ascending aorta resisting dissection. Positive ER immunohistochemistry may guide the surgeon to consider the radical resection of dilated ascending aorta.

PS-12-012

Immunohistochemical characteristics of aortic valve in the case of atherocalcinosis

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Objective: According to the results of the Euro-Heart Survey on Vascular Heart Disease the most common pathology is nonrheumatic aortic stenosis, it is also called as calcific aortic valve stenosis (CAVS), as in its pathogenesis the process of biomineralization of valve cusps and ring plays the main role.

Method: 30 samples of mineralized aortic valves (I group) and 10 samples of aortic valve without evidence of biomineralization (II group - control) were studied. Immunohistochemical study of expression of collagen I, CD68, MPO, S100A9, caspase 3 and osteopontin was conducted in AV tissue of both groups.

Results: In CAV tissues the fibrillar component (collagen I) growths was found, but the quantitative compositions of circulating inflammatory cells (CD68+) are not significantly different from the control group. CAVs contain much more MPO+ -cells ($p < 0.001$) in comparison to the group of AV without biomineralization. Our data show a significant increase of the S100A9 and OPN expression in the mineralized tissue of AVs ($p < 0.01$). Also a higher expression level of Casp3 and MPO was found in CAVs ($p < 0.05$).

Conclusion: High Casp 3 expression confirms the increased level of cell elimination in the CAVs tissue, which is obviously connected with the impact of high local concentrations of S100A9. These facts can contribute to the development of pathological biomineralization of AV. Since osteopontin inhibits the hydroxyapatite formation by binding to the surface of the crystals, its hyperproduction is a counteracting factor against biomineralization in AV tissue.

PS-12-013

Post-mortem pathological investigation of early myocardial damage: A review of fluorescent markers and immunohistochemical procedures

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Objective: Post-mortem diagnosis of early ischemic lesions of the myocardium is a key issue in forensic pathology. This study present the prominent histochemical and immunohistochemical methods and analyse their diagnostic accuracy and the potential timeframe of their use.

Method: An extensive literature review has been conducted using electronic databases of peer-reviewed international journals, textbooks and guidelines. We emphasized in the selection of comparative studies between various markers from cases with varying post-ischemia intervals to facilitate the differential analysis of their distribution patterns and the temporal evolution of their biological substrates and therefore signal.

Results: Acridine-orange and hematoxylin-eosin autofluorescence are the main fluorescent markers in use, with the former showing satisfactory sensitivity and specificity after 2 h of ischemia. The immunohistochemical detection of cellular proteins depletion [H-FABP, desmin, myoglobin, troponin C and T] was found to begin early and correlate with the ischemic process well. On the other hand, fibronectin and fibrinogen deposition requires a longer postischemic period and yields spatially different results. Finally, the visualization of the C5b-9 complement complex on and in myocytes sets in 30–40 min after the onset of ischemia.

Conclusion: The integrated combination of these markers combined with the research on fast post-mortem analysis of cryosectioned tissue should improve our diagnostic potential.

PS-12-014

Evaluate fibrous loosening of cardiovascular tissues due to ageing

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Objective: Due to fibrous loosening by ageing, aortic dissection, valvular regurgitation, and cord rupture of mitral valve occur. We have tried to evaluate degree of loosening by the values of speeds-of-sound(SOS) which has strong correlation with tissue stiffness. Do SOS through tissues correspond to tissue loosening? Which chemical changes happen at the site of loosening?

Method: We compared the SOS images between lesions and normal areas. To investigate the sensitivity to protease digestion, we compared the SOS images before and after digestion. To detect chemical changes of

the tissues, lysyl oxidase (LOX), fibronectin (FN), and vitronectin (VN) were stained by specific antibodies.

Results: The lesions of aortic dissection, valvular regurgitation, and cord rupture of mitral valve showed slower SOS than the surrounding normal areas and were vulnerable to protease digestion. LOS stainings were weak and FN and VN stainings were stronger compared with the surrounding tissues.

Conclusion: The degree of fibrous loosening corresponded well to the reduced values of SOS. In chemical alteration, cross-linking between collagen fibers decreased and matrix proteins such as FN and VN increased in amount.

PS-12-015

A rare case of primary cardiac osteosarcoma: The importance of the pathological diagnosis

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Objective: Most tumours arising from the heart are benign and when malignant, they tend to be metastatic. Primary cardiac osteosarcoma is a very rare entity which accounts for less than 10 % of primary malignant heart tumours and is generally located at the left atrium.

Method: A 70-year-old female patient presented with a nodular mass of the left atrium, clinically resembling myxoma. No past medical history or further symptoms were mentioned. The mass was excised and pathological examination followed.

Results: Sections showed a spindle cell neoplasm with a fascicular architecture and moderate or high cellularity. The neoplastic cells were highly pleomorphic and atypical. Abundant mitoses were found. Tumour cells produced large amounts of osteoid matrix. Chondroid differentiation was evident, as well. Immunohistochemical panel, including vimentin, AE1/AE3, CK8/18, EMA, CD99, CD31, calretinin, SMA, desmin, S100 and CD34 revealed vimentin positivity of the neoplastic cells. Bone scan and thoracic-abdominal computed tomography were followed, which did not show any signs of distant metastasis or another primary tumour. Nine months later, the patient is free of disease.

Conclusion: The pathological diagnosis of primary cardiac osteosarcoma is of great importance for the patient, because it is usually misdiagnosed as myxoma clinically.

PS-12-016

The influence of clinical determinants on aortic diameters - an autopsy morphometric study

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Objective: The authors compared aortic diameters in relation with patients' gender and age.

Method: The studied material consisted of aortic cross sections at four different levels (the ascending aorta—AscAo, the aortic arch—AoArch, the distal thoracic aorta—DTAo and the abdominal aorta—AbdAo) fixed in buffered formalin from 91 patients deceased during hospitalization and autopsied. The mean diameter of each section was determined with specially designed image analysis software.

Results: The men had larger mean diameters than women in all four sections. All assessed aortic mean diameters were increasing with age. AscAo diameter had the most obvious increasing, while AbdAo diameter had a mild progression with age.

Conclusion: Aortic dimensions undergo a remodeling process influenced by gender and the ageing process. There was no other autopsy study to present reference values of the aortic segments diameters therefore further studies on larger series are required to validate these observations.