Faculty of Medicine of Palacký University Olomouc

XXXIV. CONFERENCE OF STUDENT'S SCIENTIFIC ACTIVITY

Olomouc, 29. – 30. 5. 2001

Selected Abstracts

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ENDOSCOPIC DIAGNOSTICS AND TREATMENT OF UPPER DIGESTIVE TRACT HEMORRHAGE

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Key words: Gastrointestinal hemorrhage / Hematemesis / Melena / Interventional endoscopy / Endoscopic Hemostasis

BACKGROUND

Upper digestive tract hemorrhage is still a severe and often life-threatening acute condition. On June 1, 2000 new clinical guidelines on comprehensive care of patients with gastrointestinal hemorrhage in Olomouc District became effective. The regulations concerned with both emergency preadmission and hospital care aimed at improving care quality and organization. The aim of our retrospective study was to describe endoscopic diagnostics and therapy in Olomouc District (the population of 226,000) in 2000. The study is a part of retro-prospective evaluation of the clinical guidelines.

METHODOLOGY

The retrospective analysis included patients examined for revealed signs of acute hemorrhage from upper digestive tract between January 1, 2000 and December 31, 2000 at the Department of Endoscopy, 2nd Internal Medicine Clinic.

RESULTS

During the observed period 2,306 upper digestive tract endoscopies were performed, including 372 acute. Of those, 310 acute esophagogastroduodenoscopies for revealed signs of upper gastrointestinal hemorrhage were performed. 262 patients were examined, i. e. 1.18 investigations per patient, 159 of them (60.7 %) were males and 103 (39.3 %) females. The average age was 62.0 years (a 19–95 year span, SD ± 17.1), with the median of 65 years. 102 patients (38.9 %) were younger than 60 and 160 (61.1 %) were older than 60 years of age. The causes for examination included melena in 161 cases (55.5 %), hematemesis in 103 (35.5 %), hematochesia in 18 (6.2 %), collapse in 4 (1.4 %) and shock in 4 (1.4 %). Lesions with stigmas of recent hemorrhage and active bleeding lesions were localized in esophagus (27.4 %), stomach (37.1 %) and duodenum (35.5 %). Lesions with no signs of bleeding were observed in 123 examinations (39.7 %), lesions with signs of recent hemorrhage in 65 (21.0 %) and active bleeding lesions in 122 (39.3 %). The source specifications and bleeding activities of individual lesions are shown in Tab. 1. 162 endoscopic treatments were performed – injection sclerotherapy with 1.5 % Aetoxysclerol in 143 cases (88.3 %), injection sclerotherapy with 96 % alcohol in 9 (5.6 %), hemoclip in 8 (4.9 %), thermocoagulation in 2 (1.2 %). Primary hemostasis was achieved in 155 cases (95.7 %). Hemostasis was not successful in 7 patients (4.3 %). 3 patients had duodenal bulb active bleeding – type Forrest Ia, 2 had peptic ulcer type Forrest Ia hemorrhage, 1 had Forrest Ib duodenal bulb ulcer bleeding and 1 esophageal varices bleeding. In 2 of the patients consequent hemostasis was successful, in both cases after hemoclip placement. One case was type Forrest Ia peptic ulcer active bleeding lesion, the other type Forrest Ib duodenal bulb ulcer. 5 patients underwent further therapy at the surgical ward, 1 patient after successful following hemostasis of type Forrest Ia peptic ulcer bleeding at the 2nd Internal Medicine Clinic ICU. One patient was examined at the Clinic of Anesthesiology and Resuscitation. In 2 patients it was not possible to perform endoscopic localization of the source due to severe bleeding and they were referred to urgent surgical intervention. In patients younger than 60 years of age lesions with no signs of bleeding were diagnosed in 52 examinations (40.3 %), lesions with signs of recent hemorrhage in 29 (22.5 %) and active bleeding lesions in 48 examinations (37.2 %). In patients older than 60 lesions with no signs of bleeding were diagnosed in 71 examinations (39.2 %), lesions with signs of recent bleeding in 36 (19.9 %) and active bleeding lesions in 74 examinations (40.9 %).

CONCLUSIONS

Acute gastroscopy is most often performed after melena and hematemesis. The correlation between bleeding activity and symptoms is significant for hematemesis only. The most common source of upper digestive tract hemorrhage is peptic lesions – 54 %. Primary endoscopic hemostasis was achieved in 95.7 % of cases. The bleeding activity – age relationship is not significant (p = 0.755). Most patients with active bleeding lesions were hospitalized at the internal ward ICU after performed gastroscopy – 60.4 %.

Table 1. The source specifications and bleeding activities of individual

Lesion	no signs of bleeding		with stigmas of recent hemorrhage		active bleeding lesions		total *n*	
Esophageal varices	11	35.5 %	4	12.9 %	16	51.6 %	31	100 %
Esophageal ulcer	5	50.0 %	2	20.0 %	3	30.0 %	10	
Esophagitis	65	85.5 %	4	5.3 %	7	9.2 %	76	
Mallory-Weiss tear	2	13.3 %	0		13	86.7 %	15	
Hiatal hernia	127	98.4 %	1	0.8 %	1	0.8 %	129	
Fundal varices	3	100.0 %	0		0		3	
Gastric ulcer	14	23.0 %	21	34.4 %	26	42.6 %	61	
Gastritis	12	100.0 %	0		0		12	
Congestive gastopathy	21	87.5 %	1	4.2 %	2	8.3 %	24	
Hemorrhagic gastropathy	38	74.5 %	4	7.8 %	9	17.7 %	51	
Gastric tumour	6	50.0 %	3	25.0 %	3	25.0 %	12	
Bulb varices	0		0		0		0	
Duodenal ulcer	14	17.3 %	28	34.6 %	39	48.1 %	81	
Teleangiektazie	1	100.0 %	0		0		1	
Other	11	47.8 %	5	21.7 %	7	30.5 %	23	

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THE ROLE OF PROGRAMMED CELL DEATH AND THE GENES INVOLVED IN REGULATION OF PROGRAMMED CELL DEATH IN DIFFERENTIATION OF HUMAN EMBRYO MYOCARD

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Key words: Apoptosis / Macrophages / Heart

During the last ten years the research has focused on defining the basic principles of apoptosis, a process which is complementary but antagonistic to proliferation. Proof of the enormous importance of apoptosis in embryonic development is a specific term of programmed cell death (which has been given and which is used in biology). It indicates that the genetic equipment of each cell includes information for a system of receptors, transducers and effectors, co-operation of which results in removal of undesirable cells during development.
The aim of our work was to compare the sensitivity of methods for detecting apoptosis, expression of its regulation proteins and immunohistochemical proof for macrophages in embryonic myocard.
We worked with 9 human embryos and foetuses between the 6th and the 22nd week of IUD. We assessed quantitatively labelling and apoptotic indices (LI and AI) by means of graphic analysis system ACC 4.0. For proving the presence of cells which had undergone apoptosis we used the following methods: TUNEL, APOSTAIN and LAMIN-B. The results of these three methods were compared. Proliferative proteins Ki-67 and PCNA and apoptosis regulating proteins P53 and BCL-2 were detected by means of an indirect three-step immunohistochemical method. The same one was used for the proof of macrophages using monoclonal antibody NCL-CD68-KP1 to antigen CD68 in lysosomal membranes.
We demonstrated expression of all the studied proteins in developing myocard. The expression of PCNA increased in two periods (from the 8th to the 11th and the 18th to the 20th of IUD), especially in the compact layer (LI 0,2–0,3). Expression of Ki-67 increased as well, but LI was lower (0,02–0,17). In proteins P-53 and BCL-2 there was very low LI in all the studied stages of development. AI was quite high in myocard, especially in spongious level of ventricles in a 9-week-old foetus (0,55). In the 14th and the 18th weeks of IUD AI was higher in the spongious layer (0,53) than in the compact one (0,35). The high level of apoptosis and expression of proliferation proteins reflects the fundamental reconstruction of the wall of the developing human myocard.
We showed the presence of cells having antigen CD68 in their lysosomal membranes in the developing myocard as well and we assume these cells collaborate in the removal of cells which had undergone apoptosis. Apoptosis and its regulation proteins has a very important role in the differentiation of human myocard and they participate in the formation of the heart anlage.

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THE DETECTION OF MACROPHAGES INVOLVED IN CLEARANCE OF APOPTOTIC CELLS IN HUMAN DEVELOPING KIDNEY

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Key words: Macrophages / Apoptosis / Nephrogenesis

According to recent research on mice, though less on the human material, cells responsible for clearing away apoptotic cells during development are not only *non professional* phagocytes (as neighbouring epithelial cells or endothelial cells of embryonic blood vessels) but also tissue-fixed macrophages.
The aim of our work was the detection of such macrophages in mesenchymal interstitium in neogenous zone of human metanephros.
Histologically normal kidneys were collected from 7 embryos and fetuses ranging from the 8th–21st week of gestational age. Tissues were routinely processed. The detection was performed by means of the standard indirect three-step immunohistochemical method using murine monoclonal antibody NCL-CD68-KP1 to the antigen CD68 localized on lysosome membranes. Quantitative evaluation was carried out by means of graphic analysis system ACC 4.0 and labeling indices were determined (LI = the rate of CD68 positive cells and all the cells in observed area).
CD68 positive cells were quantified in mesenchymal intesticium in neogenous zone of metanephros where apoptotic cells were found as mentioned in our previous papers. CD68^{+} macrophages appeared dispersely in all the ages studied. Values of LI reached the maximum in the 11th and 13th weeks of IUD. In the 18th and 21st weeks there were only single positive cells. The presence of CD68 positive cells indicates their involvement in the clearance of apoptotic cells. However, this issue requires further investigation (e.g. double staining for the proof of apoptotic bodies engulfed by macrophages).

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INTEROCCLUSAL REGISTRATION USING A GOTHIC ARCH TRACING

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Key words: Gothic arch tracing

The aim of this study is to determine the relationship between results of interocclusal registration using a gothic arch tracing and the position of the patient.
Measurements of interocclusal relationship were carried out by using a registration device number 100 for maxilla (maxillary plate with a stylus) and number 110 for mandible (mandibular registration plate) developed by Condylator-Service. The registration device was attached to individual basal acrylic plates fixed by clasps to the teeth arch. The position of the central bearing point was determined by measuring the distances to two previously defined points on the registration plate. 10 measurements were performed on the patient with his head being in the same direction

as the axis of his body and 11 measurements were performed on the patient with his head bent backwards. The anteroposterior difference of the central bearing point position was assessed mathematically using Heron's formula.
The 0.44 millimetres progression of the position of the central bearing point on the registration plate (i.e. mandible was moving backwards) was observed at the patient's position with his head bent backwards. Results were statistically analysed and are significant at the 5% level (two tailed t-test).
This study proved that the position of the patient has a significant influence at the results of interocclusal registration using a gothic arch tracing. Presented findings are of significance when dealing with new types of dental chairs, where the position of the patient is changed to an important degree.

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ECHOGRAPHY IN GRAVE'S ORBITOPATHY

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INTRODUCTION

Grave's orbitopathy the most common cause of unilateral or bilateral proptosis is autoimmun thyreogenic dissease. Early diagnosis markedly helps to evaluate severity of patien's condition and start helpfull complex therapy. One of the examination techniques is echography. We evaluate muscle thickness their internal structure and reflectivity of orbital fat.

AIMS

The aim of our study was to evaluate the benefit of echografic examination in determination of Grave's orbitaopthy diagnosis.

METHODS

We examined 38 patients (76 eyes) suspicies of Grave's orbitopthy. Their age was between 19–69, 10 males, 28 females. Both patients with new detected thyroid dysfunction and patients observed for this dissease were included. The grade of proptosis we evaluated with Hertl's exophtalmometer and the muscle thickness we measured by echography (internal rectus muscle). The value of proptosis over 20 mm and with over 55 mm we considered to be patognomic for Grave's orbitopathy.

RESULTS

Proptosis had 39 % of patients, thickness of internal rectus muscle had 58 % of patients. Both proptosis and thickned internal rectus muscle we found in 32 % and 25 % of patients had normal values. That means that in 26 % of patients Grave's orbitopathy shouldn't be diagnosed without use of echography.

CONCLUSION

Echography is invaluable examination for diagnosis and observing patological changes in Grave's orbitopthy at this time.

THE CONTRIBUTION OF IMMUNOPHENOTYPIC AND MOLECULAR CYTOGENETIC METHODS FOR THE DIAGNOSIS OF MANTLE CELL LYMPHOMA

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INTRODUCTION

Mantle cell lymphoma (MCL) represents about 6 to 8 % of all non-Hodgkin's lymphomas (NHL). MCL is derived from naive pre-germinal centrocytes, which are localized in primary lymphoid folicles and in the mantle zone of secondary folicles. Cytologically, MCL consists of small to medium lymphoid cells with irregular and indented nuclei, coarse chromatin and conspicious nucleoli (classic variant). A blastic variant of the lymphoma is also recognized, characterized by larger neoplastic cells, finely dispersed chromatin and small nucleoli. Nodal involvement in MCL usually shows diffuse or nodular monotonous lymphoid proliferation. In rare cases, nodularity may be prominent and may be misinterpreted as a follicular lymphoma. The t(11;14)(q13;q32) chromosomal translocation is a characteristic cytogenetic alteration. This translocation involves the locus of the immunoglobulin heavy chain on chromosome 14 and the bcl-1 gene on chromosome 11 and results in overstatement of PRAD1 gene. The gene encodes cyclin D1 controlling cell cycle (G_1–S transition). The lymphoma is usually disseminated at diagnosis and the clinical course is agressive. MCL is resistant to our conventional chemotherapeutic regimens. Mantle cell lymphoma is an often misdiagnosed entity, due its morphological variability. In this study we analyzed the contribution of modern immuno-phenotypic, cytogenetic and molecular-genetic methods to diagnostic accuracy.

PATIENTS

We analyzed the data of 56 patients diagnosed between January 1995 and June 2000. The patients were predominantly male (61 %), the median age was 63 years. 96 % of the patients had an advanced stage of the disease (Ann Arbor), with B-symptoms (61 %) and >1 extranodal organ involvement (73 %) and bone marrow involvement (96 %). Anemia (<120g/l) was present in 46 % of cases and peripheral lymphocytosis (>4*10^9/l) in 61 %. Tumor marker levels (LDH, $ß_2$-microglobulin, thymidine-kinase) were elevated in 62 %, 84 %, and 86 % respectively.

METHODS

The evaluated parameters at diagnosis included complete medical and disease history, physical examination, complete blood count with differential, serum chemistry panel, serum tumor markers (LDH, $ß_2$-microglobulin, thymidin-kinase), chest radiograph, CT scan of the thorax, abdomen and pelvis, bone marrow aspiration/biopsy and lymph node biopsy or biopsy of possibly involved extranodal sites. The peripheral blood films and bone marrow aspirates were stained with May-Grünwald Giemsa. Immunophenotype was performed on the preparations of peripheral blood and bone marrow with the panel of leukocyte monoclonal antibodies. Specimens were analysed on the Coulter Epics XL flow cytometer. Lymph node biopsy was performed in 35 patients. The initial diagnosis was made by a local and reviewed by an expert pathologist. Biopsy specimens were stained with hematoxylin-eosin and with using immunohistologic methods. Cytogenetic and molecular-genetic metods included conventional chromosomal analysis, fluorescence in situ hybridi-

zation (FISH), comparative genomic hybridization (CGH) and polymerase chain reaction (PCR).

RESULTS

In 21 patients the diagnosis was made after examination of bone marrow and peripheral blood (leukemic form MCL, unavailable lymph node). Lymph node histology was made in 35 patients. 14 of them (40 %) had incorrect initial diagnosis: most frequently the specimens were classified as follicular lymphoma. We detected typical immunophenotype (sIg+/CD5+/CD19+/CD23-) in all patients with present tumor mass. FISH detected typical t(11;14)(q13;q32) translocation in 76 % (16/21) of cases. CGH identified additional anbalanced chromosomal changes in 76 %. The 17p- deletion was observed in 29 % (6/21). The bcl-1 rearrangement in MTC region was detected by PCR assay only in 24 %. New laboratory methods can improve diagnostic accuracy in mantle cell lymphoma, which is important for the treatment stategy. Early indicated intensive therapeutic modalities, combination of chemotherapy with imunotherapy (rituximab) and stem cell transplantation may play a role in improving the outcome, especially in younger patients.

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ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION FAILURE: COMPARISON OF PATELLAR BONE-TENDON-BONE INTERFERENCE SCREW FIXATION AND HAMSTRING EXTRAARTICULAR SCREW FIXATION

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Key words: Knee / ACL / Failure

Between May 8, 1996 and December 31, 2000, 889 anterior cruciate ligament (ACL) reconstructions were performed at the clinic where two techniques were used and compared. Better results were achieved when the hamstring extraarticular screw fixation technique was used.

INTRODUCTION

The knee joint is the most complex joint of the human body and compared to other joints it has many distinctive features. Knee joint stability is ensured by ligament and muscular system but unlike other large lower limb joints, the joint surface shape is of less importance which is why the ligament system is so massive. Knee joint stabilizers are divided into static (ligaments and 2 menisci) and dynamic (muscles). The normal knee joint function is mainly ensured by ACL and ACL ruptures most often occur during rotation movements.

AIM

To compare failures in the two ACL reconstruction techniques, to ascertain failure causes and the operation-failure time span.

PATIENTS AND METHODS

Between May 8, 1996 and December 31, 2000 889 anterior cruciate ligament (ACL) reconstructions were performed at the Clinic of Orthopedics in Olomouc. Hamstring extraarticular screw fixation was used in 543 cases and patellar bone-tendon-bone (B-T-B) interference screw fixation in 330 cases. Of all reconstructions, 66 failures occurred in 63 patients, with repeated failure in 3 patients. 45 patients were males, 21 patients females, with an average age of 24.3 years, ranging from 16 to 35 years. Right knee failure was more common – 36 cases compared to 30 cases of left knee failure. Data analysis was performed using the Chi-Square test.

RESULTS

The patients were divided into 3 groups according to the operation-failure time span. The first group consisted of 11 patients with ACL reconstruction failure within less than 90 days after operation. One failure occurred due to patients' inappropriate limb workload. 35 patients in the second group were those with ACL reconstruction failure occurring 90 to 365 days after operation. That is the most critical period for the failure and a surgeon's fault should also be considered. In 20 patients (the third group) the failure occurred more than one year after an operation. At that time the healed graft has the quality of a completely healthy ACL. Statistical comparison of the two methods revealed that the hamstring technique failed in 5.5 % and the B-T-B technique in 10.4 % of reconstructions ($p = 0.0068$). Of all 889 reconstructions 7.24 % failed, and this corresponds with results published by renowned institutions abroad.

CONCLUSION

Far better results were achieved using the hamstring extraarticular screw fixation technique compared to B-T-B technique. Future development will be observed.

THE DEVELOPMENT OF PSYCHOSOCIAL THERAPY FOR SCHIZOPHRENIC PATIENTS AT THE CLINIC OF PSYCHIATRY AND MEDICAL PSYCHOLOGY IN OLOMOUC

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INTRODUCTION

With regard to the multifactorial genesis of schizophrenic psychoses and the varied range of symptoms (both positive and negative) characteristic of the disorder, a multidimensional approach to treatment is necessary. During the acute phase of the disorder with expressed productive symptoms drug therapy prevails exclusively. However, after the cessation of productive symptoms the psycho- and sociotherapeutic processes become more important. The main objective of sociotherapeutic measures is to prevent social handicaps or, if need be, to keep them at a minimal level. Psychosociotherapeutic methods have to be applied as soon as possible after the cessation of the acute phase.

Our clinic continuously tries to create a system of aftertreatment, rehabilitation and resocialization of patients suffering from psychotic illnesses (mainly schizophrenic and schizoaffective psychoses) with the intention of improving mental state life quality of young patients.

METHODS

On March 1, 1995 a day clinic with a capacity of 12–15 clients was opened at the clinic. This offers a whole-week patients' programme based on Roder's integrated psychotherapeutic programme (IPTP), focusing mainly on the therapy of attentionally perceptive and cognitive disorders typical for schizophrenia as well as on specific deficiencies in general social behaviour. The clients of the day clinic are both clinical inpatients and outpatients from psychiatric and psychological facilities in and outside Olomouc. The programme also involves psychoeducation in following themes: signs of illnesses, prodromal syndromes and side effects of drugs.

In 1998–1999 the day clinic performed a survey of health condition including life quality in patients included in the programme. The results showed that after a 3-month period (not seen in scales) the subjects restructure their attitudes and acquire starting points for general possibility of improvement later seen in scales. The clients are able to make social contacts with therapists and friends and return to their former interests. Some clients find a new job or decide to study which is a proof of compliance.

The daily centre activities have been extended by those of a new psychosocial centre (PSC) opened on March 7, 2001 with a capacity of 12–15 clients. The PSC offers a programme for 3 days a week. The morning session is followed by a literature club, social skills training or English lessons. After some time other activities will be involved – music therapy, relaxation techniques, computer program based training of cognitive functions, PC courses, yoga, a theatre club, visits to cultural events and sports activities. Thus the programme stimulates memory improvement, increases concentration abilities, supports emotional experiences and – last but not least – facilitates social contacts establishment.

An essential component of the PSC therapy is patients' participation in the centre's organization. The group functions as a closed one, partly as an opened one. One of the patients is the so called guarantor – this means that he or she makes sure that everything necessary for the particular day has been prepared, informs the others in case the programme has been cancelled or accepts the apologies of those who are unable to come. The PSC professionals' roles are more those of consultants or supervisors. They also closely cooperate with final-year students of medicine and psychology and other volunteers taking active part in guiding particular activities and working with the clients. The volunteers were also helpful when we investigated the clients' difficulties in socializing caused by their unemployment and loss of everyday contacts.

CONCLUSION

The programme is largely dependent on the participation of volunteers introducing new approaches to the therapy thanks to the informal character of the interaction. On the other hand social reintegration of schizophrenic patients helps in the destigmatization of schizophrenic disorders in social awareness.