FIBROSIS IDENTIFIED IN THE BONE MARROW BIOPSIES OF PATIENTS WITH ESSENTIAL THROMBOCYTHEMIA: ITS INCIDENCE AND SIGNIFICANCE FOR THE DIFFERENTIAL DIAGNOSTIC CONSIDERATIONS

Marcinek J., Plank L., Szépe P., Balhárek T.

Department of Pathology, Comenius University, Jessenius Medical Faculty and Martin's Faculty Hospital, Martin, Slovakia

Summary

Myelofibrosis (MF) may develop in all types of myeloproliferative disorders and its identification is of clinical relevance. Typical bone marrow (BM) morphology of patients with essential thrombocythemia (ET) shows either "normal" amount or "a slight increase" of reticulin fibers, but the published data differ in relation to the applied MF definition and ET diagnostic criterias. The aim of this study was to evaluate retrospectivelly MF in BM biopsies of 30 cases in which the diagnosis of ET was confirmed also clinically by local hematologists. In 7 of the patients not only primary but also sequential biopsy was available. The MF grade and extent were evaluated semiquantitatively in archival slides stained by Gömöri silver impregnation. The analysis was based on the European clinico-pathological criteria 2004 (ECP) defining a) normal bone marrow fibrosis (MF0), b) slight reticulin fibrosis (MF1), c) advanced reticulin and initial collagen fibrosis (MF2) and d) advanced collagen fibrosis (MF3). Generally, in majority of the biopsies MF0 (n = 6) or MF1 (n = 25, 18× focal and 7× diffuse) was found. More advanced MF2 was much less common as it was present in 6 biopsies (5× focal and 1× diffuse). In relation to the actual time of BM biopsy during course of the disease, the introductory biopsies done at the time of diagnosis (n=18) showed 3× MF0, 14× MF1 and 1× MF2. The biopsies performed after a long time of patients observations (n = 12) showed 3× MF0, 7× MF1 and 2× MF2. In 5 of 7 sequential biopsies the progress of MF was evident, but 4 of these patients were treated by cytoreductive therapy. We conclude that the BM of patients with ET in initial phase shows either MF0 or focal slight increase of reticulin fibers (MF1). In addition, the long course of the disease and/or applied therapy may lead to more developed MF and more advanced MF stages (diffuse MF1 or MF2). Therefore their finding in the BM biopsies examined in the later phases of the disease should not exclude the diagnosis of ET.

Key words: myelofibrosis - essential thrombocythemia - bone marrow - reticulin and collagen fibers

Súhrn

Výskyt myelofibrózy a jej význam pri bioptickej diagnostike esenciálnej trombocytémie

Myelofibróza (MF) sa vyskytuje pri všetkých typoch myeloproliferatívnych ochorení a jej prítomnosť má dôležitý diferenciálne diagnostický význam. Klasický morfologický obraz kostnej drene (KD) pacientov s esenciálnou trombocytémiou (ET) sa vyznačuje normálnym množstvom, alebo len ľahkým zmnožením retikulínových vlákien, avšak konkrétne údaje o výskyte sa líšia v závislosti od použitých diagnostických kritérií ET či kritérií hodnotenia stupňa MF. Cieľom našej práce je retrospektívna analýza stupňa MF v bioptických vzorkách 30 pacientov, u ktorých bola diagnóza ET potvrdená i klinicky, v spolupráci so spádovými hematológmi. V 7 prípadoch sme mali k dispozícii okrem primárnych biopsií i sekvenčné rebiopsie KD. Stupeň a rozsah MF sme hodnotili semikvantitatívne v archivovaných preparátoch vyšetrených pomocou Gömöriho impregnačnej metodiky. Pri hodnotení MF sme použili najnovšie Európske klinicko-patologické kritériá z roku 2004 (ECP), ktoré rozoznávajú: a) normálne množstvo fibrózy v KD (MF0), b) ľahkú retikulínovú fibrózu (MF1), c) pokročilú retikulínovú fibrózu s počínajúcou kolagénovou fibrózou (MF2), d) rozvinutú kolagénovú fibrózu (MF3). Vo väčšine biopsií bol identifikovaný stupeň MF0 (n = 6) alebo MF1 (n = 25, 18× fokálne, 7× difúzne). Pokročilejší stupeň myelofibrózy (MF2) sa vyskytoval zriedkavejšie – v 6 biopsiách (5× fokálne, 1× difúzne). Ak sa zohľadňuje trvanie ochorenia, tak v počiatočných bioptických vzorkách odobratých v čase diagnózy ochorenia (n = 18) bola 3× identifikovaná MF0, 14× MF1 a 1× MF2. V skupine biopsií získaných po dlhodobom sledovaní pacientov (n = 12) bola prítomná 3× MF0, 7× MF1 a 2× MF2. V 5 zo 7 sekvenčných biopsií KD bola zaznamenaná progresia MF (4× po predchádzajúcej cytoredukčnej terapii). Preto možno konštatovať, že v KD pacientov s ET v počiatočných štádiách ochorenia sa nachádza normálne množstvo fibrózy (MF0), alebo len ľahké zmnoženie retikulínových vlákien (MF1). Dlhodobý priebeh ochorenia či použitie terapie vedie k progresii rozsahu či stupňa MF (difúzna MF1 alebo MF2), a preto ich výskyt v KD v pokročilejších štádiách ochorenia nevylučuje diagnózu ET.

Kľúčové slová: myelofibróza – esenciálna trombocytémia – kostná dreň – retikulín – kolagén

Čes.-slov. Patol., 44, 2008, No. 3, p. 62–66

INTRODUCTION

An increase of reticulin and collagen fibers as a result of reactive connective tissue deposition in the hematopoietic bone marrow (BM) is traditionally called bone marrow fibrosis or myelofibrosis (MF) (9). It shows a step-wise evolution from a physiologically "normal" state through first minimal focal and latter on diffuse increase of reticulin fibers up to the formation of collagenous fibers in advanced stages of the process, associated in some of the cases with osteomyelosclerosis (5, 19). In contrast to fine isolated

reticulin fibers, the collagenous fibers do not appear in the "normal" BM (2, 21). The etiopathogenesis of MF is rather complex, however, in majority of the cases it is related to a synthesis of various growth factors which stimulate the proliferation and synthetic activity of BM fibroblasts causing myelofibrosis (13).

MF may appear in the course of many hematological and non-hematological BM disorders and in principle it may be either primary or secondary (3, 25). A primary MF showing tendency to progress to collagen fibrosis and myelosclerosis is an obligatory sign of the primary chronic idiopathic myelofibrosis; this entity represents a part of the spectrum of chronic Ph1- myeloproliferative disorders (CMPD). In contrast, there are considerable differences in the frequency and grade of fibrotic changes in other CMPD types (22). The secondary MF is less often developing in the course of chronic myelogenous leukemia (6) and of polycythemia vera (10). In patients with essential thrombocythemia (ET), fibrosis of the bone marrow seems to be rare and is generally considered to be unusual for this disease (11). In majority of the published series, only single ET cases showing limited fibrosis have been described. In addition, it seems to be generally and world-wide accepted that the non-treated patients with ET do not develop apparent and advanced collagenous BM fibrosis. Therefore the histopathologic finding of advanced fibrosis observed in the trephine BM biopsies of patients showing clinical, laboratory and histopathologic signs of CMPD in its chronic phase is considered to testify rather against the diagnosis of ET (15, 24).

However, in our routine praxis we have been aware of some diagnostic problems related to these definitions. That was the reason for us to undergo a retrospective clinicopathological analysis of BM biopsies of patients with ET from our register to reevaluate the extent and the grade of eventual fibrotic changes.

MATERIAL AND METHODS

For the purpose of a more complex retrospective evaluation of the consecutive BM biopsies of 213 CMPD patients diagnosed according to the WHO criteria (11) in our register (in the period of 21 months), questionnaire formulars were sent to the responsible hematologists to ask them to describe the course of the disease and to formulate their opinion on the final diagnosis of the CMPD type. The final diagnosis of ET was confirmed clinically in 30 patients examined during the period (out of 148 received answers) and all the BM biopsies of these patients were included in the complex retrospective analysis. For other purposes also other parameters of the BM morphology were re-evaluated, however, this study was focused on the association of BM fibrosis with ET only.

There were 20 males and 10 females in this cohort of patients, their age at the time of biopsy diagnosis ranged from 20 to 79 years (median of 55.9 years). The clinical indications to perform the trephine BM biopsy were following: a/ an incidental and short-time observation (up to 12 months) of the thrombocytosis in 18 cases, b/ the thrombocytosis observed within a longer period (2-23 years with median of 7.4 yers) in 10 patients and c/ to follow up the state of BM hematopoiesis in 2 patients with known history of previous diagnosis of ET. In addition, in 7 patients sequential BM biopsies were available, performed in the interval of 1 month to 9 years after the primary BM biopsy (median 35 months).

All the BM biopsies were taken from the posterior iliac crest with the Jamshidi trephine needle, fixed in 10% formaldehyde solution and decalcified in the EDTA solution for 24 hours. The biopsy specimens were embedded in paraffin, cut into 4-5 micrometers sections and stained by HE, PAS reaction, Giemsa staining and Gömöri silver impregnation. For the retrospective assesment of MF, two independent observers (JM and LP) used the semiquantitative grading system according to the "European clinico-pathological criterias" (ECP) (21). This system identifies following grades of BM fibrosis (figures 1-4): MF0 - normal amount of reticulin fibres, MF1 - slight reticulin fibrosis, MF2 - advanced reticulin fibrosis accompanied by the first signs of collagenous fibrosis and MF3 - coarse reticulin and developed collagen fibrosis. In addition to the grading, we distinguished also the extent of the myelofibrosis: the focal fibrotic changes appearing in small areas of individual bone marrow spaces of the whole examined specimen ("patchy fibrosis") versus diffuse changes being identified in the majority or in all examined bone marrow spaces.

Altogether, the study included reevaluation of the presence, extent and grade of BM fibrosis in 37 BM biopsies of 30 patients with a clinically testified diagnosis of CMPD of ET type. The final results were related to the stage of the disease, e.g. into the group of BM biopsies taken in the initial versus biopsies examined in the advanced and/or posttherapeutic stages.

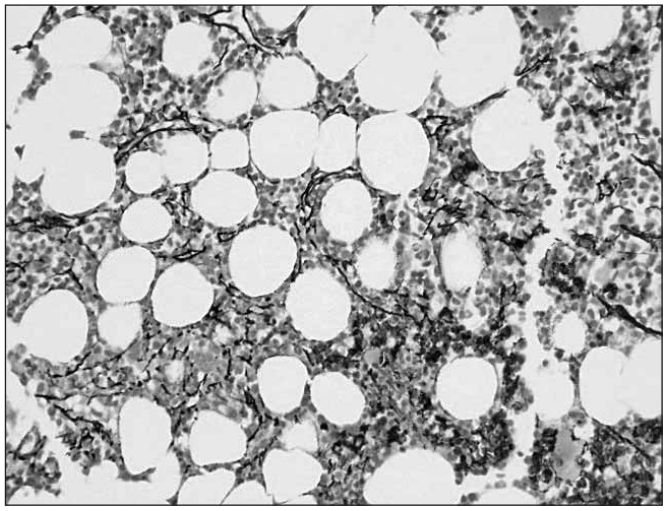


Fig. 1: Normal bone marrow fibrosis (MF0) – fine scattered reticulin fibres without intersections, rings of fibres enclosing vessels. Gömöri impregnation, 200x

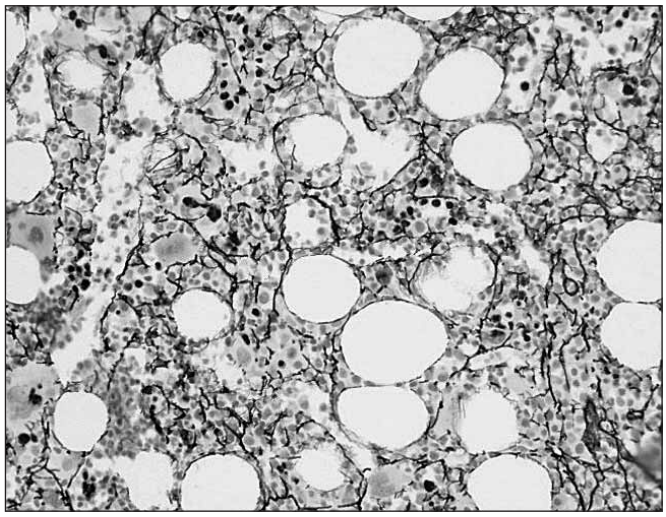


Fig. 2: Slight reticulin myelofibrosis (MF1) – loose network of fine reticulin fibres with intersections. Gömöri impregnation, 200x

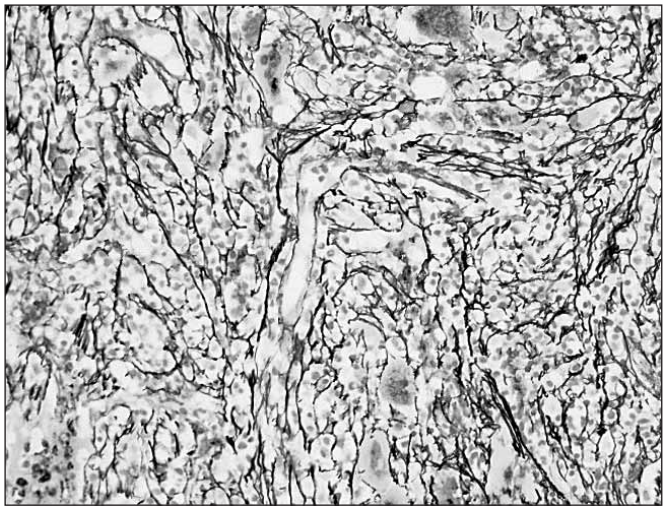


Fig. 3: Advanced reticulin myelofibrosis (MF2) – diffuse network of thicker reticulin fibres with extensive intersections. Gömöri impregnation, 200x

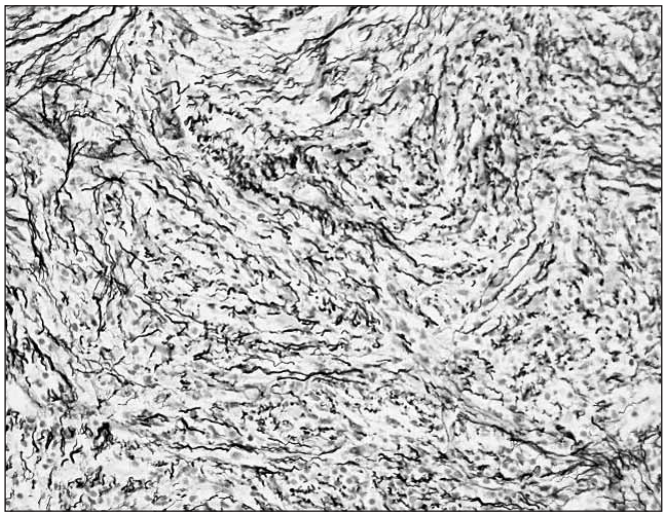


Fig. 4: Advanced collagenous myelofibrosis (MF3) – dense network of coarse reticulin and collagen fibres forming bundles, apparent reduction of hemopoiesis. Gömöri impregnation, 200x

RESULTS

The results of the study are summarized in table 1. A "normal" amount of reticulin fibers graded as MF0 was identified in 6 BM biopsies (16.2% of all the biopsies). The quantitative and qualitative parameters of reticulin fibers identified in 25 BM biopsies (67.6% of all) fulfilled the criteria of bone marrow fibrosis grade MF1; in 18 of them (48.7%) the MF1 fibrosis was focal and in 7 (18.9% of all) diffuse. In 6 BM biopsies (16.2% of all the biopsies) the fibrosis was of grade MF2, in 5 of these cases (13.5%) it was focal and in 1 (2.7% of all) diffuse. Advanced collagen fibrosis or osteosclerosis (MF3) were not identified.

Within the group of 18 patients whose BM biopsies were examined in the initial phase of the disease, grade MF0 was observed in three, focal MF1 in twelve, diffuse MF1 in two and focal MF2 in one biopsy.

Within the group of 12 patients whose BM biopsies were examined for the first time examined in the advanced phase of disease (10 patients in a long follow up and 2 patients with previously hematologically diagnosed ET), MF0 was found in 3, focal MF1 in 5 and diffuse MF1 in 2 BM biopsies. In addition, one BM biopsy showed focal and one diffuse MF2 grade of fibrosis.

In 7 patients sequential biopsies were available to compare the findings in the initial versus in the advanced stages of the disease. In one case the MF1 grade remained unchanged. The biopsies of 5 patients showed a progress of either grade and/or extent of the fibrosis: in two patients progress from MF1 focal into MF1 diffuse, in one patient from MF1 diffuse into MF2 focal and in two patients from MF1 focal into MF2 focal. The sequential biopsies of the only one patient showed decrease of the grade of the diffuse fibrosis from MF2 into MF1.

DISCUSSION

By studying the data on myelofibrosis occurring in ET patients, one has to realize and understand that it is difficult to compare the data obtained by different working groups using heterogenous criteria for MF and ET definition and obtained after previous different therapeutical approaches. The historical data on incidence of BM fibrosis in patients with ET are rather heterogenous because they reflect the contemporary "historically appropriate" opinions, definitions and criteria for individual types of CMPD, incl. the criteria of ET definition. Some authors have observed MF of various degree in 20-50% of ET patients (3, 8, 25), including the occurence of collagen fibrosis (8). These relativelly high figures reflect the use of previously used old-fashioned "exclusive clinical diagnostic criterias for ET" according to PVSG ("Polycythemia Vera Study Group" - 20). These criteria e.g. did not recognize the prefibrotic stage of chronic idiopathic myelofibrosis and mixed these early stages of primary myelofibrosis with ET changes (25).

More recent data on bone marrow histopathology of ET patients have identified a relatively rare occurence of the diffuse reticulin fibrosis - in the time of diagnosis in 0-6% of the cases (6, 10, 12). However, by using a more restricted assessment of MF, some data incl. previous observations from our register demonstrated MF in up to 21% cases of ET (1). In the presented group of patients we have identified significantly higher occurence of bone marrow myelofibrosis of

Table 1: Fibrosis in the bone marrow of patients with essential thrombocythemia

	Grade of MF	MF0	MF1		MF2		MF3
	No. of biopsies		focal	diffuse	focal	diffuse	
New diagnosed ET	18	3	12	2	1	0	0
Long time follow up	10	3	4	1	1	1	0
Previously diagnosed ET	2	0	1	1	0	0	0
No. of sequential biopsies	7	0	1	3	3	0	0
Total	37	6	18	7	5	1	0

ET patients, however predominantly in the form of slight focal reticulin fibrosis (MF1), which is consistent with the minimal increase of reticulin fibres often observed also by at least some other authors in the initial phase of disease (15, 16).

According to evaluation of the follow-up biopsies examined in a 3 to 5 years interval after the initial diagnosis of ET in the series of different working groups, the progress of MF during the course of the disease seems to be rare – it was reported in 1.5-6.6 % of cases (7, 10, 12). In contrast, Buhr et al. (6) observed in a 4-years follow up of 300 patients with ET only one case with a documented progress of MF. In our study we have identified relatively high percentage of cases showing secondary development of reticulin fibrosis. However, in two of these patients the progress of MF could be a natural part of long course of the disease (7, 16), as the rebiopsies were performed in the late advanced stages of the disease – after 5, resp. 12 years. The progress of MF might also be related to the applied therapy of the disease in at least 4 from 5 patients, because the cytoreductive therapy of ET (Busulphan and Interferon) is known as a causative agent leading to progress of bone marrow myelofibrosis (23). Even in some older studies evaluating the effect of Busulphan therapy, the MF development was recognized in almost ¼ of the cases (18).

In the recent period, when diagnostic criteria of the prefibrotic stage of chronic idiopathic myelofibrosis were generally recognized, the differences might be related also to the approach how to define ET – whether morphologically or clinically. In a majority of the published series the selection of the patients seems to be done almost exclusively on basis of BM histomorphology, as only limited clinical and laboratory data were available (1, 3, 6, 8, 10, 12, 25). In contrast, our series includes patients with diagnosis of ET established by local hematologists, who possess all available clinical or laboratory data, including results of our original BM biopsy examination and who had the possibility to observe the clinical behavior, symptomatology or progress of the disease. However, a disadvantage of this way of patients selection is represented by a possibility of false ET diagnosis, especially in the cases with a short follow up. For all these cases, the time for the disease observation might not be sufficient to confirm or to exclude definitively the diagnosis of ET or of some other Ph1- CMPD type.

In addition, another factor influencing the final results obtained by various investigators seem to be represented by the applied criteria of MF definition and its grading system. Kreft et al. (12) didn't describe any MF in the time of ET diagnosis, however they used a peculiar grading system for MF. According to their criteria, the occurence of collagen fibres was necessary for MF1 grade (12), but according to grading system used also by us this finding corresponds to the MF2 grade. Moreover, Kreft et al. did not consider the increase of reticulin fibers as a reliable sign of initial MF (12), but the majority of authors (including us) consider the increase of reticulin fibres as a part of MF1 grade (1-3, 5-7, 9-11, 15, 18-25). On the other hand, Adamkov et al. (1) used a 5-step grading system with more restricted criteria for MF0. Their approach means that so called first grade of MF according to Adamkov et al. (1) often corresponds to "normal bone marrow fibrosis" (14). Also the „Hannover diagnostic criteria" for MF used by a working group of Georgii (5,6,10) are almost identical with the ECP criteria (14). However, both systems are semiquantitative and so hampered by subjectivity and by personal skills and experiences of investigators, as well as by various methods of tissue processing (4).

The results of our analysis seem to confirm the opinion, that the initial phase of ET is usually accompanied by a finding of a "normal" amount of reticulin fibres in BM. However, in agreement with ECP criteria for ET (17), in a majority of the cases a slight and focal reticulin fibrosis might be observed. After a long follow-up of ET and/or after its cytoreductive therapy, the bone marrow may show advanced stages of MF, represented by diffuse reticulin fibrosis resp. collagen fibrosis. In contrast, our results demonstrate that the advanced bone marrow fibrosis is rarely detected in biopsies of patients in initial phases of the disease.

In agreement with the recent data of several leading authors in this field (6, 10, 11, 17) it seems to be plausible to conclude that a correct BM biopsy diagnosis of ET requires evaluation of the BM morphology in a complex manner. The main stress should by paid to identify the typical ET morphology including the appropriate BM cellularity with the for ET typical morphology of megakaryocytes (17, 24). However, it is necessery to emphasize, that the finding of slight reticulin fibrosis at the time of diagnosis or the progress of MF in the course of disease or after therapy, resp. after cytoreductive therapy does not exclude the diagnosis of ET.

Supported by: Grant of Comenius University Nr. 84/2007

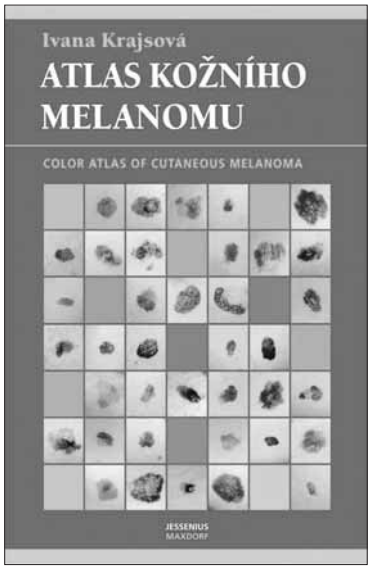
LITERATURE

1. **Adamkov M., Plank L., Szépe P.:** Incidence of myelofibrosis among individual types of chronic myeloproliferative disorders. Brat. Lek. Listy, 99, 1998, s. 240-244.
2. **Bauermeister D.E.:** Quantitation of bone marrow reticulin – A Normal Range. Am. Jour. Clin. Pat., 56, 1971, s. 24-31.
3. **Brunning R.D., McKenna R.W.:** Chronic myeloproliferative diseases. In: Brunnig R.D., Mc Kenna R.W., ed. Atlas of Tumor Pathology – Atlas of the Bone Marrow, Washington: AFIP, 1994, s. 195-254.
4. **Buesche G., Georgii A., Kreipe H.H.:** Diagnosis and quantification of bone marrow fibrosis are significantly biased by the pre-staining processing of bone marrow biopsies. Histopathology, 48, 2006, s. 133-148.
5. **Buhr T., Büsche G., Choritz H., Länger F., Kreipe H :** Evolution of myelofibrosis in chronic idiopathic myelofibrosis as evidenced in sequential bone marrow biopsy specimens. Am. J. Clin. Pathol., 119, 2003, s. 152-158.
6. **Buhr T., Georgii A., Choritz H.:** Myelofibrosis in chronic myeloproliferative disorders. Incidence among subtypes according to the Hannover classification. Path. Res. Pract., 189, 1993, s.121-132.
7. **Cervantes F., Alvarez-Larran A., Talarn C., Gomez M., Montserrat E.:** Myelofibrosis with myeloid metaplasia following essential thrombocythaemia: actuarial probability, presenting characteristics and evolution in a series of 195 patients. Br. J. Haematol., 118, 2002, s. 786-790.
8. **Duhamel G., Stachowiak J.:** Bone marrow fibrosis in malignant hemopathies and cancers. Histological study of 2786 biopsies. Semm. Hop., 57, 1981, s. 111-116.
9. **Frisch B., Bartl R.:** Myelofibrosis and osteosclerosis and other fibroses in the bone marrow. In: Frisch B., Bartl R. ed. Biopsy Interpretation of Bone and Bone Marrow. Edward Arnold, 1999, s. 244-256.
10. **Georgii A., Buhr T., Büsche G., Kreft A., Choritz H.:** Classification and staging of Ph-negative myeloproliferative disorders by histopathology from bone marrow biopsies. Leukemia and Lymphoma, 22, 1996, s. 15-29.
11. **Imbert M., Vardiman J.W., Pierre R., Brunning R.D., Thiele J., Flandrin G.:** Essential thrombocytaemia. In: Jaffe E.S., Harris N.L., Stein H., Vardiman J.W., ed. World Health Organization Classification of Tumors, Pathology & Genetics, Tumours of Haemopoietic and Lymphoid Tissues, Lyon: IARC Press, 2001, s. 39-41.
12. **Kreft A., Büsche G., Ghalibafian M., Buhr T., Fischer T., Kirkpatrick C.J :** The incidence of myelofibrosis in Essential thrombocythemia, Polycythemia vera and Chronic idiopathic myelofibrosis. A retrospective evaluation of sequential bone marrow biopsies. Acta Haematol., 113, 2005, s. 137-143.
13. **Lev P.R., Marta R.F., Vassallu P., Molinas F.C.:** Variation of PDGF, TGFbeta, and bFGF levels in essential thrombocythemia patients treated with anagrelide. Am J Hematol., 70, 2002, s. 85-91.

14. **Marcinek J., Plank L.:** Chronická idiopatická myelofibróza: biologická charakteristika a diagnosticky a prognosticky relevantný histopatologický „grading“ fibrózy. Trans. a hemat. dnes, 12, 2006, s. 62-69.
15. **Michiels J.J.:** Diagnostic criteria of the myeloproliferative disorders (MPD): Essential thrombocythaemia, Polycythemia vera and Chronic megakaryocytic granulocytic metaplasia. Net. J. Med., 51, 1997, s. 57-64.
16. **Michiels J.J., Juvonen E.:** Proposal for revised diagnostic criteria of Essential thrombocythemia, and Polycythemia vera by the Thrombocythemia Vera Study Group. Sem. In Throm. and Hemost., 23, 1997, s. 339-346.
17. **Michiels J.J., Kvasnicka H.M., Thiele J.:** Chronic Ph^1-negative myeloproliferative disorders (MPDs). In European MPD Workshop, Rotterdam, 2004, s. 2-40.
18. **Van de Pette J.E., Prochazka A.V., Pearson T.C., ., ., .:** Primary thrombocythemia treated with busulphan. Br. J. Haematol., 62, 1986, s. 229-237.
19. **Thiele J., Hoeppner B., Zankovich R., Fischer R.:** Histomorphometry of bone marrow biopsies in Primary osteomyelofibrosis/sclerosis (Agnogenic myeloid metaplasia) - correlations between clinical and morphological features. Wirchows Archiv A Pathol. Anat., 415, 1989, s. 191-202.
20. **Thiele J., Kvasnicka H.M.:** Chronic myeloproliferative disorders with thrombocythemia: a comparative study of two classification systems (PVSG, WHO) on 839 patients. Ann. Hematol., 82, 2003, s. 148-152.
21. **Thiele J., Kvasnicka H.M., Facchetti F., Franco V., Van der Walt J., Orazi A.:** European consensus on grading bone marrow fibrosis and assessment of cellularity. Haematologica, 90, 2005, s. 1128-1132.
22. **Thiele J., Kvasnicka H.M., Fischer R.:** Histochemistry and morphometry on bone marrow biopsies in Chronic myeloproliferative disorders - aids to diagnosis and classification. Ann. Hematol., 78, 1999, s. 495-506.
23. **Thiele J., Kvasnicka H.M., Niederle N., et al.:** The impact of Interferon versus Busulphan therapy on the reticulin stain-measured fibrosis in CML-a comparative morphometric study on sequential trephine biopsies. Ann. Hematol., 70, 1995, s. 121-128.
24. **Thiele J., Kvasnicka H.M., Zankovich R., Diehl V.:** Relevance of bone marrow features in the differential diagnosis between Essential thrombocythemia and early stage of Idiopathic myelofibrosis. Haematologica, 85, 2000, s. 1126-1134.
25. **Vardiman J.W.:** Chronic myelogenous leukemia and the Myeloproliferative disorders. In: Knowles D.M., ed. Neoplastic hematology, Baltimore: Williams Wilkins, 1992, s. 1405-1438.

Address for correspondence:

MUDr. Juraj Marcinek,
Department of Pathology,
Comenius University, Jessenius Medical Faculty and Martin's Faculty Hospital, Kollárova 2, 036 59 Martin, Slovakia.
Phone Nr.: +421-43-4133002, mail: marcinek@jfmed.uniba.sk



ATLAS KOŽNÍHO MELANOMU

Color atlas of cutaneous Melanoma

Ivana Krajsová

Melanom patří mezi velmi závažné kožní nádory. Jeho prognóza přitom zcela zásadně závisí na tom, v jakém stadiu je stanovena diagnóza, resp. na tom, kdy lékař vysloví na tuto diagnózu podezření. Právě v počátečních stadiích může být rozpoznání melanomu dosti obtížné a vyžaduje velkou vizuální zkušenost. S cílem pomoci dermatologům i praktickým lékařům v základní diagnostice tohoto velmi zhoubného onemocnění nyní vychází dvojjazyčný obrazový atlas obsahující několik set fotografií, které dokumentují nejrůznější typy a stadia melanomu. Autorkou atlasu je naše přední odbornice v dermatoonkologii. Základní orientaci v problematice melanomu čtenář může najít v monografii této autorky Melanom, (nakladatelství Maxdorf v roce 2006).

Vydalo nakladatelství Maxdorf v roce 2008, 248 str., cena: 995 Kč, formát: B5, váz., edice Jessenius, ISBN: 978-80-7345-151-6.

Objednávky můžete posílat na adresu: Nakladatelské a tiskové středisko ČLS JEP, Sokolská 31, 120 26 Praha 2, fax: 224 266 226, e-mail: nts@cls.cz. Na objednávce laskavě uveďte i jméno časopisu, v němž jste se o knize dozvěděli.