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*Case Report*

# Clonal cytogenetics changes in progression of multiple myeloma to extramedullary relapse and plasmocellular leukemia: a case report

Jan Smetana[1,2,3], Petr Kuglik[1,3], Henrieta Greslikova[2], Renata Kupska[2], Pavel Nemec[2], Aneta Mikulasova[1,2], Iveta Valaskova[3], Jan Oppelt[4,5], Martina Almasi[2,6], Marta Krejci[7], Zdenek Adam[7], Ludek Pour[7], Roman Hajek[2,8]

*[1]Laboratory of Molecular Cytogenetics, Institute of Experimental Biology, Faculty of Science, Masaryk University, Brno, Czech Republic; [2]Babak Myeloma Group, Department of Pathological Physiology, Faculty of Medicine, Masaryk University, Brno, Czech Republic; [3]Department of Medical Genetics, University Hospital, Brno, Czech Republic; [4]CEITEC-Central European Institute of Technology, Masaryk University, Brno, Czech Republic; [5]National Centre for Biomolecular Research, Faculty of Science, Masaryk University, Brno, Czech Republic; [6]Department of Clinical Hematology, University Hospital, Brno, Czech Republic; [7]Departmnet of Internal Medicine-Hematooncology, University Hospital, Brno, Czech Republic; [8]Faculty of Medicine, University of Ostrava and University Hospital Ostrava-Poruba, Ostrava, Czech Republic*

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**Abstract:** Extramedullary relapse (EM) is an aggressive form of the disease with a dismal outcome. We present cytogenetic findings of a 52-year-old female with MM, which progressed rapidly into plasmocellular leukemia and extramedullary subcutaneous tumor in the head. At the time of diagnosis, G-banding showed hypotriploid karyotype (63-64 chromosomes) and using cIg-FISH we found translocation t(4;14)(p16;q32) and gain(1)(q21). At the time of disease progression, the same chromosomal abnormalities were present in the bone marrow, peripheral blood and the EM lesion: del(13)(q14), del(17)(p13), t(4;14)(p16;q32) and gain(1)(q21). Before progression, array-CGH showed, hyperdiploid karyotype with trisomies of chromosomes 2, 3, 7, 8, 9, 11, 17, 18, 19 and 20, while after progression non-hyperdiploid karyotype was detected with additional structural deletions in 1p, 2p, 4q, 11p, 12p, 13, 14q, 17p, 22q and homozygous deletion in 1p32.3. In addition, deep resequencing of TP53 gene showed presence of 2 known mutations in exon 6(c.632C>T) and exon 7(c.700T>C). In summary, EM relapse of this patient was connected to a change of the entire genome profile. Extramedullary lesion most probably originated by an expansion of one clone of tumor plasma cells from the bone marrow, which was confirmed by identical genomic profile of both tested samples. Thus, change of ploidy status should be considered as potential hallmark of adverse course of the disease.

**Keywords:** Multiple myeloma, extramedullary relapse, clonal evolution, genetic changes, ploidy switch, TP53 mutations

## Introduction

Multiple myeloma (MM) is characterized by malignant proliferation and accumulation of clonal plasma cells (PCs) in bone marrow, formation of osteolytic lesions and presence of monoclonal immunoglobulin in serum and/or urine [1].

Extramedullary relapse of MM (EM) is defined by the presence of extraskeletal clonal plasma cells infiltrates. EM can be present either at the time of initial MM diagnosis (primary EM) or at the time of MM relapse (secondary EM). The PCs may infiltrate into soft-tissues or be connected to the bone [2]. Patients with soft-tissue infiltrates have very poor prognosis even in the era of new drugs [3]. It is known that development of MM is characterized by clinical and biological heterogeneity caused by proliferation of best adapted clone(s) of PCs, which is driven by mechanisms based on Darwin's theory of evolution of species. Keats *et al*. showed that genetic characterization of MM subclones by array-CGH technique is a suitable approach for evaluation of clonal development and incidence

of high-risk genetic signatures [4]. In addition, deletion of *TP53* locus in 17p13.1 area is known to be important hallmark of potential risk of development secondary plasma cell leukemia (sPCL) [5, 6]. Recent data also showed that incidence of del(17)(p13.1) is associated with the presence of mutations in remaining allele in *TP53*, which could ultimately lead to complete inactivation of the gene [7, 8]. Thus, evaluation of presence of cytogenetic abnormalities on genome-wide level during the course of the disease could bring novel information about pathogenesis of MM and help with the risk assessment for patients. In addition, data obtained from next generation sequencing (NGS) techniques in MM diagnosis already bring additional insights into individual tumor characterization and tracking clonal evolution over time [9].

In this study, we describe cytogenetic findings observed in a younger female patient with aggressive MM, which evolved into plasma cell leukemia and extramedullary MM within 4 years after diagnosis. Progression of the disease was accompanied by ploidy switch from hyperdiploid MM detected during diagnosis to non-hyperdiploid MM and acquired loss of *TP53* gene, which was observed in extramedullary tissue and in PCs infiltrated into peripheral blood. Moreover, targeted resequencing of *TP53* exons 4-11 showed development and switch in incidence of mutations in *TP53* gene in different stages of the disease.

## Patients and methods

Female patient was diagnosed with MM in the Department of Internal Medicine-Hematooncology (IHOK), University Hospital Brno, in 11/2007. Patient's biological material was obtained after she signed the informed consent form approved by the Ethical committee of the hospital. The bone marrow aspirates for cytogenetics analyses were prepared according to standard procedure as described previously [10]. The cIg-FISH samples were prepared according to FICTION protocol from Ahmann et al. with slight modifications [11]. The enriched samples of PCs for genomic profiling were obtained by anti-CD138+ immunomagnetic beads (AutoMACS Pro, Miltenyi Biotec GmbH, Bergisch Gladbach, Germany) or by fluorescent-activated cell sorting (FACS Aria, BD Biosciences, San Jose, CA, USA), as described previously [12].

### *FISH evaluation*

The following FISH panel of commercial DNA probes was used for analysis: LSI IGH/FGFR3 Dual Color Probe, LSI 13q14 (RB1) Spectrum Green Probe, LSI p53 (17p13.1) Spectrum Orange Probe and LSI D5S23/D5S721, CEP 9, CEP 15 Multi-Color Probe Panel (Abbott Laboratories, Abbott Park, IL, USA). Detailed FISH protocol was described elsewhere [13]. Hyperdiploidy was defined as gain of at least two of three evaluated chromosomes in a single cell. Gain(1)(q21) was evaluated by home-made probe using fluorescent labeled bacterial artificial chromosome (BAC) (clone RP11-205M9); protocols for BAC isolation and labeling were followed from online resources of University in Bari, Italy (http://www.uniba.it). Slide preparation and FISH analyses were performed according to manufacturer's protocols. We used cut-off values recommended by the European Myeloma Network [14].

### *Array-CGH analysis*

Genomic DNA was isolated from purified PCs by Qiagen Core Kit A (Qiagen) according to manufacturer's recommendation. Whole genome screening of copy number alterations (CNAs) was performed with Agilent Human 4 × 44 k and 1 × 244 k microarrays according to manufacturer's protocol with slight modification described previously by us [15]. Agilent Genomic Workbench 7.0.4 was used for aberration calling according to previously described settings [16]. Microarray data are available in the ArrayExpress database (www.ebi.ac.uk/arrayexpress) under accession number E-MTAB-3577.

### *TP53 sequencing*

Targeted resequencing of *TP53* gene was made with SeqPlate TP53 system (Roche). The SeqPlate TP53 enables sequencing of exons 4 to 11 of the human TP53 gene where single nucleotide polymorphisms (SNPs) associated with hematological malignancies has been found. The SeqPlate TP53 was used to generate 8 amplicons with emulsion PCR (emPCR) and sequenced using the Roche GS Junior Sequencing System. Data were aligned to NCBI Reference Sequence: NC_000017.11 using Burrows-Wheeler Alignment Tool (BWA) soft-

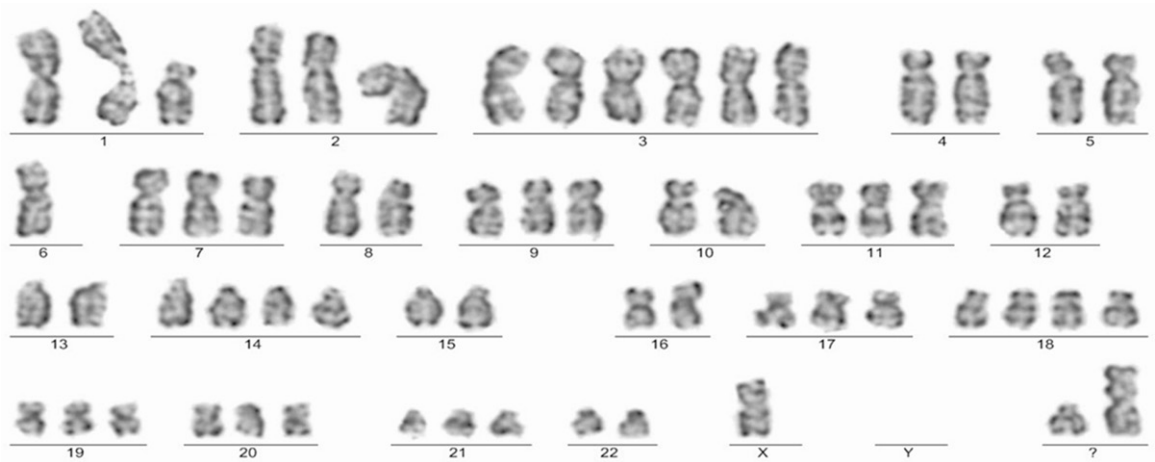

**Figure 1.** Hypotriploid karyotype from patient with EM relapses at the time of diagnosis detected by G-banding: 63, X, -X, -X, der(1), +3, +3, +3, -4, -5, -6, -6, -8, -10, -12, -13, +14, -15, -16, +18, -22, +mar, +mar.

**Table 1.** Chromosomal aberrations evaluated by FISH in patient with EM myeloma during the disease

| Time of sample aspiration | FISH evaluations | | | | | |
|---|---|---|---|---|---|---|
| | *del(13)(q14) loss of RB1* | *del(17)(p13) loss of TP53* | *IgH rearrangement* | *t(4;14)(p16;q32) translocation IgH/FGFR3* | *gain(1)(q21) gain of CKS1B* | *Hyperdiploidy (+5, +9, +15)* |
| New diagnosis | neg. | neg. | 97% poz. | 76% poz. | 97% poz. | 76%, +9 |
| 1. relapse | neg. | neg. | 68% poz. | 50% poz. | 94% poz. | 93%, +9 |
| 2. relapse | neg. | neg. | 81% poz. | 81% poz. | 100% poz. | 64%, +9 |
| progression | 70% poz. | 67% poz. | 88% poz. | 77% poz. | 45% poz. | NH |
| EM PCs | 97% poz. | 92% poz. | 91% poz. | 69% poz. | 91% poz. | NH |
| EM tumor mass | 73% poz. | 70% poz. | 74% poz. | NA | 72% poz. | NH |
| PCL | 96% poz. | 96% poz. | 92% poz. | 76% poz. | 73% poz. | NH |

EM - extramedullary relapse; PCL - plasma cell leukemia; NA - not available.

ware (http://bio-bwa.sourceforge.net/bwa.shtml). For SNP calling and filtering was used GATK HaplotypeCaller (www.www.broadinstitute.org/gatk) and data were visualized in Integrative genomics viewer (IGV) and processed according to published recommendation [17]. Sequencing data are available in the ArrayExpress database (www.ebi.ac.uk/arrayexpress) under accession number E-MTAB-3600.

## Results

Female patient was diagnosed in 11/2007 at the age of 48 years with symptomatic MM (CRAB positive), Durie-Salmon stage III. A, ISS stage 3. At the time of diagnosis, multiple osteolytic lesions of skull, 50-90% infiltration of bone marrow with PCs, presence of lambda light chains in both serum (4.6 g/l) and urea (19.9 g/l), $\beta_2$microglobulin level was 9.25 mg/l were found. The patient received 4 cycles of CAD regiment (cyclophosphamide-doxorubicin-dexamethasone) together with support therapy using bisphosphonate (zolendronat once per month) and reached VGPR (= very good partial response). Patient was then pretreated with melphalan regiment (200 mg/m$^2$) with following first ASCT (05/2008) and reach stable VGPR.

Cytogenetic evaluation by FISH technique was performed during all stages of the disease. At the time of the diagnosis, conventional G-banding showed hypotriploid karyotype (**Figure 1**) with additional copies of chromosomes 2, 3, 7, 9, 11, 14, 17 and 21, gain 1q arm and missing copy of chromosome 6. These findings were partially verified by the cIg-FISH evaluations (gain 1q21, +17). *IGH* locus rearrangement and translocation t(4;14) were also observed.

Patient first relapsed in 03/2009 after detection of higher level of lambda light chains in urea. Patient was treated by CTD regi-


**Figure 2.** Graphical overview of CNAs from array-CGH technique in EM patient after second relapse. Whole-genome screening showed hyperdiploid karyotype consisted of trisomies of chromosomes 2, 3, 8, 9, 11, 17-20 and 22. Structural gains of genetic material were observed in 1q, 6p, 7p, 13q, 14q, 16p, 20q, 21q and Xq, whereas losses were found in 4p, 12q, 14q, Xp and Xq.

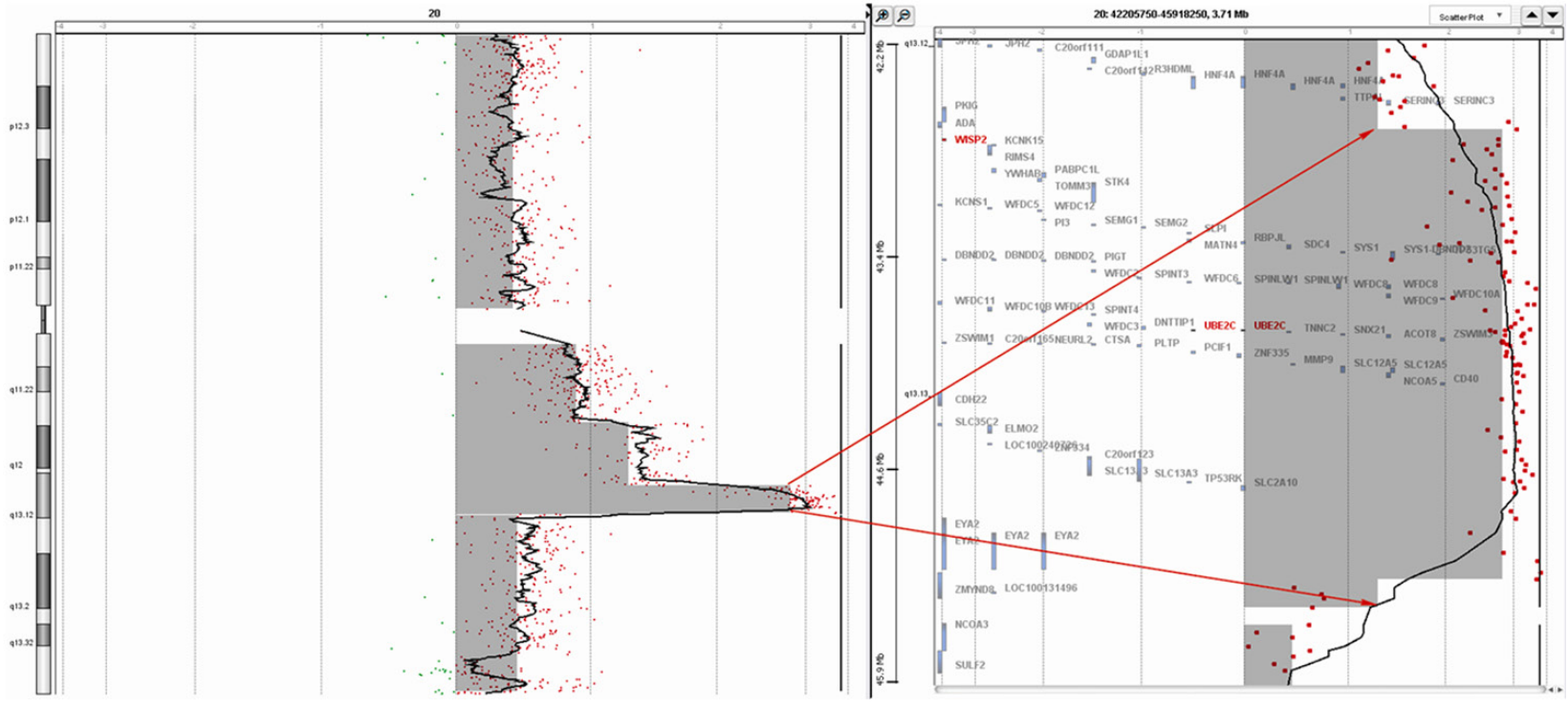


**Figure 3.** Overview of CNAs affected chromosome 20 in PCs sample after second relapse. Left part of the picture is representation of copy number profile of chromosome 20, while right part shows region of DNA amplification in 20q13 of 2.6 Mb in size (determined by red arrows) including loci of two potential protooncogenes *WISP2* and *UBE2C* (highlighted).

men (Cyclophosphamide-Thalidomide-Dexamethasone), but due to intolerance to Thalidomide, this therapy was terminated, and patient then received 4 cycles of CVD regiment (Cyclophosphamide-Velcade-Dexamethasone) and reached VGPR.

Second relapse occurred in 02/2010 accompanied by presence of higher level of lambda light chains in urea and development of anemia. Patient was treated by RCP regiment (Revlimid-Cyclophosphamide-Prednisone) followed by melphalan pretreatment (200 mg/m$^2$) and second ASCT (05/2011), after which patient reached PR (= partial remission).

Cytogenetic changes detected by cIg-FISH in first and second relapse did not change from those observed at the time of diagnosis. Presence of *IGH* rearrangement and t(4;14) was observed together with gain 1q21 and additional copy of chromosome 17 (+17) with increasing frequency between first and second relapse (**Table 1**). Additionally, array-CGH whole-genome analysis confirmed presence of extra copies of chromosomes 2, 3, 8, 9, 11, 17, 18, 19, 20 and 22 corresponding with hyperdiploid subtype of MM and revealed complex structural changes including areas of gains in 1q, 6p24.3-6pter, 7p11.1-7p22.3, 7q11.2-7q33, 13q32.1-13q34, 14q11.2-14q23.1, 16p11.2-16p13.3, 21q11.2-21q22.13, 20q11.2-20q-13.3 and losses of genetic material in 4p16.3 and 14q24-14.32.3, Xp11.1-Xpter a Xq11.1-Xq25 (**Figure 2**). Notably, we observed region of amplification (more than 10 copies) of 2.6 Mb size in 20q13 carrying at least two potential proto-oncogenes *WISP2* and *UBE2C* (**Figure 3**).

In 09/2011, extramedullar subcutaneous tumor of 4 cm in diameter located in calvaria right temporal lobe was detected with infiltration of PCs verified histologically. Furthermore, the progression to plasmocellular leukemia was diagnosed as morphological evaluation discovered presence of PCs in PB; following flow cytometry analysis detected presence of 30% PCs in PB. Complete blood count showed leukocytosis (22.5 × 10$^9$/l), anemia (Hb 58 g/l), and thrombocytopenia (2 × 10$^9$/l). Moreover, mucocutaneous bleeding manifestations were observed. The patient was treated as symptomatic without chemotherapy. Patient died due to progression of the disease in 10/2011.

The incidence of cytogenetic aberrations was evaluated from PB, BM and extramedullary tumor after progression of the disease. The presence of gain(1)(q21) and t(4;14)(p16;32) observed before progression was verified in all these types of samples. Moreover, cIg-FISH evaluation showed del(17)(p13) and del(13)(q14) associated with loss of *TP53* and *RB1* genes, respectively. Genome-wide profiling with array-CGH discovered non-hyperdiploid karyotype with large number of structural aberrations including loss of chromosomes 10 and 13, loss of 17p including loci of *TP53* in 17p-13 area and homozygous deletion in 1p32.3 (*CDKN2C, FAF1*) and 1p31. Further areas of loss genetic material were observed in 1p31.1-1p33, 2p25.1-2p25.3, 2p24.2-2p24.3, 4p16.3, 4q11-4qter, 11p13-11p15, 12p12.1-12p13.2, 12p11.2-12p12.1, 14q23-14q32.33, 16q11-16qter and 17p11-17pter, while gains occurred in 1p35.3-1p36.3, 1q21.1-1qter, 6p43.3-6pter, 19p13.1-19p13.3 a Xq25-Xq28. Notably, genomic profile from extramedullary tumor was identical with those from CD138+ cells (**Figure 4**). Thus, EM relapse of this patient was connected to a change of the entire genome profile. Detailed description of CNAs detected in patient before and after progression is available in Supplementary Table 1.

In summary, array-CGH screening showed hyperdiploid karyotype with overall 26 copy number abnormalities with the majority of trisomies and large gains of genetic material (median = 29.1 Mbp) before progression, while samples from bone marrow and extramedullar mass showed hypodiploid clone with total of 30 copy number abnormalities including monosomies of chromosomes 10 and 13 and regions of both gains and losses of genetic material. For both stages of the disease was typical presence of t(4;14) detected by FISH, gain 1q, loss of 4p16 and gain 6p25-6p24.

The sequencing analysis of *TP53* gene mutation status was made retrospectively from PCs acquired at the time of diagnosis, after second relapse and during progression of the disease together with biological material from extramedullary tissue. We observed parallel evolution of 2 mutations consistent with development of intraclonal heterogeneity in our patient. During all evaluated stages of disease was detected missense mutation in exon 6(c.63-2C>T), which frequency gradually ascended

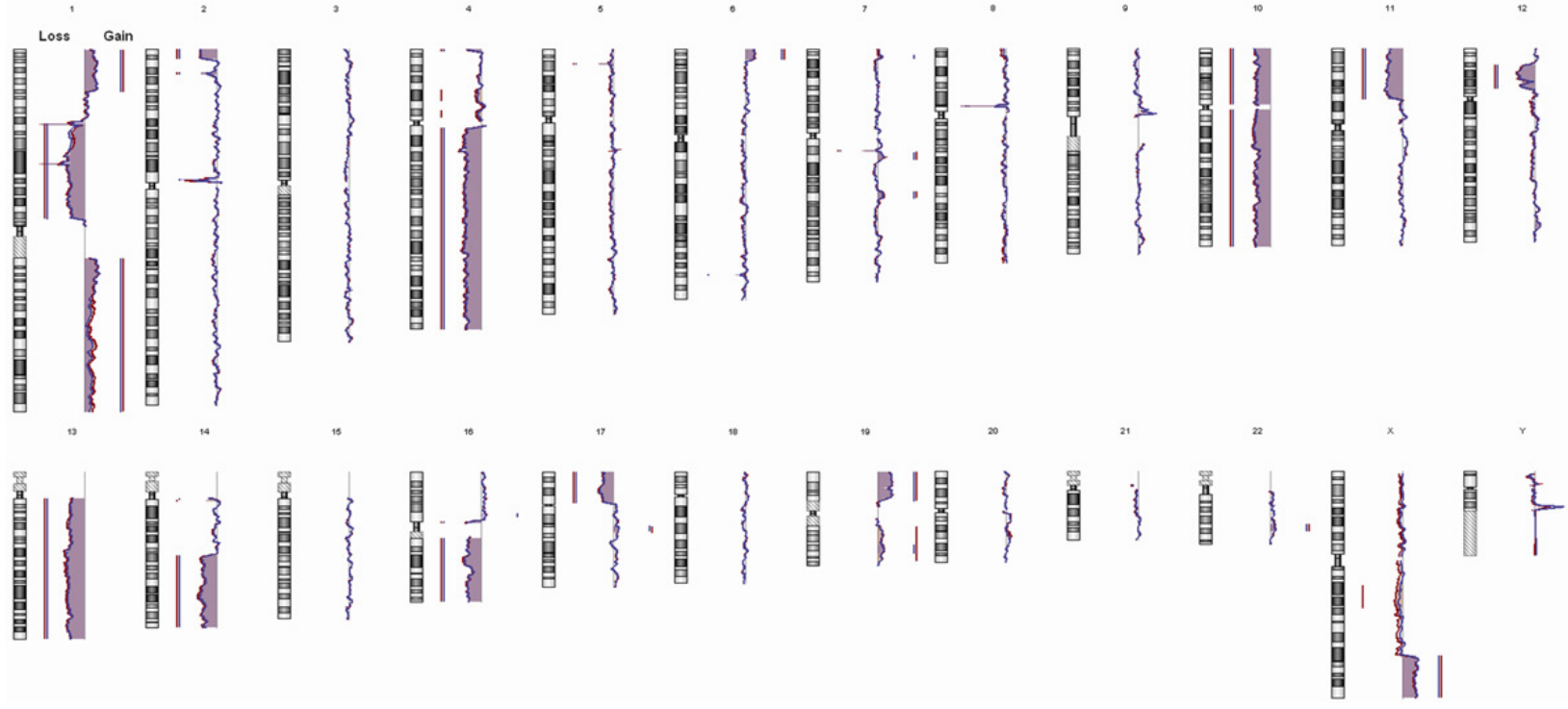


**Figure 4.** Graphical overview of CNAs from array-CGH technique in EM patient after progression. Blue color line refers to sample from extramedullary tissue; red line corresponds to sample from PCs. Whole-genome screening showed non-hyperdiploid karyotype with monosomies of chromosomes 10 and 13 together with homozygous deletions in 1p32.3 and 1p31. Structural losses of genetic material were observed in 1p33, 2p25, 2p24, 4p16, 4q, 11p15, 12p13, 12p12, 14q23; 16q and 17p, structural gains were found in 1p36, 1q; 6p25, 19p13 and Xq.

**Table 2.** Incidence of *TP53* mutations in patient with MM in different stages of disease detected by SeqPlate TP53 and Roche GS Junior system

| TP53 exon nr. | Mutation position | cDNA description | Protein description | New diagnosis | 2nd relapse | Progression | EM tumor |
|---|---|---|---|---|---|---|---|
| 6 | 632 | c.632C->T | p.T211I | 10.5% | 26.6% | 92.8% | 82.9% |
| 7 | 700 | c.700T->C | p.Y234H | 12.3% | 59.9% | 3.5% | 0.1% |

Percentages in box represents corrected variant reads. In this patient one *TP53* mutation decreased over time, while second was expands during disease development, which suggests presence of 2 clonal populations of PCs.

during evolution of the disease. On the contrary, second mutation was found in exon 7(c.700T>C). This variant occurred at the time of diagnosis and second relapse, while after progression and in extramedullary tumor was its frequency considerably lowers (**Table 2**).

## Discussion

Evaluation of chromosomal aberration is one of the most important diagnostic tools in MM diagnosis [18]. FISH technique is considered as golden standard for evaluation of high-risk features such as *IGH* translocation, loss of *TP53* gene or gain 1q21, which are known to be associated with worse prognosis and shortened survival [19]. However, utilization of genome-wide screening techniques in MM diagnosis brought crucial novel information about MM biology and development of the disease [20]. Several recent studies described and verified theory of clonal heterogeneity in MM, which ultimately leads, based on Darwinian laws, to development of the malignant clone with specific characteristics such as immortality or drug resistance acquired through accumulation of genetic aberrations [21]. In their pilot study, Keats *et al.* showed that incidence of unbalanced chromosomal changes detected by array-CGH technique in MM patients could be stable in time (good prognosis), linear (overall number of CNAs gradually increase-worse prognosis) and heterogeneous (high number of structural CNAs, incidence is changing during development of the disease-poor prognosis) [4].

In our case, we observed heterogeneous development of the MM clone. While total number of CNAs was basically the same, architecture of both genomic profiles was completely different showing hyperdiploidy before progression and hypodiploid karyotype after progression. Even though the changes of ploidy status are considered to be rare [22], previously published data showed that such cytogenetic change could be hallmark of disease progression [23], or resistance of therapy [24, 25]. Circumstances of this kind of genetic changes are only briefly described; however, it is clear that they are associated with coincidence of other high-risk aberrations, such as *IGH* translocations, loss of *TP53* gene or homozygous deletions of tumor suppressor genes [26]. Moreover, we speculate that in our patient, aggressive development after progression was mediated by presence of amplification of 20q13.12 area, carrying loci of at least two genes with known oncogenic potential (*WISP2*, *UBE2C*). After progression, other aberrations associated with adverse prognosis (loss of *TP53*, homozygous deletion in 1p32.3, monosomy 13) emerged similarly as in with previously published studies [27-30]. Identical CNAs from BM and EM samples verified that extramedullary mass and PCL had arisen from malignant PC clone originated in bone marrow.

In agreement with previous data, incidence of del(17p) as hallmark of PCL was detected after progression in PCs in bone marrow, peripheral blood and in extramedullary tissue [31, 32]. Recent studies also showed that monoallelic loss of *TP53* gene in MM patients is often associated with presence of mutations in second allele and therefore leading to very poor prognosis of the disease [33, 34]. Moreover, several studies using NGS techniques showed that linear or heterogeneous development of incidence of mutations in MM patients could be associated with adverse prognosis [35, 36]. Incidence of 2 mutations in *TP53* in our patient is an example of heterogeneous development of myeloma subclones on single gene level. Occurrence of c.632C>T was previously described in MM patients as well as in B-CLL diagnosis [7, 37], while our report of presence of c.700T>C is to best of our knowledge first in MM patients. Nevertheless, incidence of c.700T>C missense mutation was previously reported in lympho-

mas (Burkitt lymphoma, DLBCL) or patients with breast cancer [38, 39].

Both single nucleotide variant c.632C>T and c.700T>C detected in exon 6 (codon 211) and 7 (codon 234) are located in conservative part of *TP53* DNA binding domain between loop2 and loop3 [40]. It is well known that *TP53* mutations associated with poor prognosis in malignant diseases are commonly located in central core region [41, 42]. Previous studies showed that mutations in DNA binding domain could deregulate *ATM-TP53* DNA damage response pathway, which could lead to drug resistance B-CLL patients [43, 44]. Based on above-mentioned data, we speculate that incidence of those 2 mutations significantly contributed to progress of the disease of and together with presence of del(17)(p13.1) allowed rapid transformation of MM into PCL and development of extramedullary tumor.

Taken together, the utilization of array-CGH is an effective way for genomic screening of unbalanced cytogenetic changes in MM patients. Combination of FISH evaluation of *IGH* status and whole-genome profiling allowed detailed analysis of presence of unbalanced genetic aberrations at genomic level, which accompanied clonal evolution of different stages of the disease. In addition, targeted resequencing of genes with prognostic impact such as *TP53* can bring additional data critical for estimation of disease evolution. Origin of extramedullary tumor and PCL of our patient was associated with complex change of the entire genome profile and presence of c.632C>T mutation in all stages of the disease. We suppose that the extramedullary tumor originated from an expansion of one clone of tumor plasma cells from the bone marrow. This is confirmed by identical genomic profile of both tested samples. Based our findings, ploidy status acquired by genome-wide screening and targeted sequencing of *TP53* gene in del(17)(p13) positive patients should be performed in all stages of the disease in order to detect such changes, which are clearly associated with poor prognosis and shorter overall survival.

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## Disclosure of conflict of interest

None.

**Address correspondence to:** Dr. Jan Smetana, Laboratory of Molecular Cytogenetics, Institute of Experimental Biology, Faculty of Science, Masaryk University, Kamenice 5, ILBIT A3, Brno 62500, Czech Republic. Tel: +420723994704; E-mail: smetty@mail.muni.cz

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**Supplementary Table 1.** Curated aberration list of patient with MM, which evolved into PCL and extramedullary tumor extracted from array-CGH experiments

| 1) CNAs observed in samples obtained after 2nd relapse | | | | | | |
|---|---|---|---|---|---|---|
| Array type | Chromosome | Cytoband | Start | Stop | Size (Mbp) | $log_2$ ratio |
| 44 k | chr1 | q21.1-q44 | 143639135 | 247179291 | 103.54 | 0.858 |
| 44 k | chr2 | TRISOMY 2 | | | NA | 0.447 |
| 44 k | chr3 | TRISOMY 3 | | | NA | 0.790 |
| 44 k | chr4 | p16.3 | 62447 | 1848857 | 1.79 | -0.621 |
| 44 k | chr6 | p25.3-p24.3 | 204528 | 7790557 | 7.59 | 0.840 |
| 44 k | chr7 | p22.3-p11.1 | 149268 | 57613746 | 57.46 | 0.430 |
| 44 k | chr7 | q11.21-q33 | 62153588 | 132965456 | 70.81 | 0.406 |
| 44 k | chr8 | TRISOMY 8 | | | NA | 0.394 |
| 44 k | chr9 | TRISOMY 9 | | | NA | 0.754 |
| 44 k | chr11 | TRISOMY 11 | | | NA | 0.470 |
| 44 k | chr12 | q24.13-q24.23 | 111738984 | 117066270 | 5.33 | -0.442 |
| 44 k | chr13 | q32.1-q34 | 95173569 | 114029609 | 18.86 | 0.359 |
| 44 k | chr14 | q11.2-q23.1 | 19508845 | 57093625 | 37.58 | 0.780 |
| 44 k | chr14 | q24.3-q32.33 | 76303796 | 106072530 | 29.77 | -0.535 |
| 44 k | chr16 | p13.3-p11.2 | 36766 | 31726599 | 31.69 | 0.549 |
| 44 k | chr17 | TRISOMY 17 | | | NA | 0.525 |
| 44 k | chr18 | TRISOMY 18 | | | NA | 0.819 |
| 44 k | chr19 | TRISOMY 19 | | | NA | 0.868 |
| 44 k | chr20 | TRISOMY 20 | | | NA | 0.425 |
| 44 k | chr20 | q13.12 | 42724315 | 45308621 | 2.58 | 2.794 |
| 44 k | chr20 | q11.21-q13.12 | 29352138 | 45472914 | 16.12 | 1.291 |
| 44 k | chr21 | q11.2-q22.13 | 13339394 | 37560571 | 24.22 | 0.378 |
| 44 k | chr22 | TRISOMY 22 | | | NA | 0.557 |
| 44 k | chrX | p22.33-p11.1 | 2710316 | 58068490 | 55.36 | -0.788 |
| 44 k | chrX | q11.1-q25 | 61848414 | 125945620 | 64.10 | -0.828 |
| 44 k | chrX | q25-q28 | 126133062 | 154494649 | 28.36 | 0.820 |
| 2) CNAs observed in samples obtained after progression and from extramedullary tissue | | | | | | |
| Array type | Chromosome | Cytoband | Start | Stop | Size (Mbp) | $log_2$ ratio |
| 244 k | chr1 | p36.33-p35.3 | 853295 | 29132615 | 28.3 | 0.727513 |
| 244 k | chr1 | p33-p13.2 | 50805292 | 115873627 | 65.1 | -0.90605 |
| 244 k | chr1 | p33 | 50805292 | 51218298 | 0.4 | -3.30456 |
| 244 k | chr1 | p31.1 | 77934178 | 78194880 | 0.3 | -3.3695 |
| 244 k | chr1 | q21.1-q44 | 142746774 | 247190770 | 104.4 | 0.493682 |
| 244 k | chr1 | q21.1-q24.2 | 144099712 | 166620963 | 22.5 | 0.788201 |
| 244 k | chr2 | p25.3-p25.1 | 20341 | 7193424 | 7.2 | -1.0095 |
| 244 k | chr2 | p24.3-p24.2 | 16161313 | 17695680 | 1.5 | -0.98803 |
| 244 k | chr4 | p16.3 | 46772 | 1875745 | 1.8 | -0.81574 |
| 244 k | chr4 | q12-q35.2 | 53782838 | 191133668 | 137.4 | -0.93507 |
| 244 k | chr6 | p25.3-p24.3 | 97634 | 7819116 | 7.7 | 0.572371 |
| 244 k | chr6 | q25.2 | 153265300 | 154609676 | 1.3 | -0.60451 |
| 244 k | chr7 | p22.2-p22.1 | 4443438 | 6821940 | 2.4 | 0.313302 |
| 244 k | chr7 | q11.22-q11.23 | 70520169 | 75829965 | 5.3 | 0.319099 |
| 244 k | chr7 | q21.3-q22.1 | 97216432 | 102362258 | 5.1 | 0.341831 |
| 244 k | chr10 | MONOSOMY 10 | | | NA | -0.82634 |
| 244 k | chr11 | p15.5-p13 | 182372 | 34935591 | 34.8 | -0.89299 |
| 244 k | chr12 | p13.2-p12.1 | 11283811 | 22087817 | 10.8 | -0.97474 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 244 k | chr12 | p12.1-p11.23 | 24313180 | 27651419 | 3.3 | -0.89478 |
| 244 k | chr12 | q24.23-q24.31 | 119012815 | 122981124 | 4.0 | 0.368754 |
| 244 k | chr13 | MONOSOMY 13 | | | NA | -0.92982 |
| 244 k | chr14 | q11.1-q11.2 | 18504575 | 106151105 | 87.6 | -0.81091 |
| 244 k | chr16 | p13.3-p11.2 | 36766 | 33875313 | 33.8 | 0.34256 |
| 244 k | chr16 | q11.2-q24.3 | 35005009 | 88690615 | 53.7 | -0.89057 |
| 244 k | chr17 | p13.3-p11.2 | 29169 | 21720142 | 21.7 | -0.661 |
| 244 k | chr17 | q21.2-q21.31 | 22315936 | 78653589 | 56.3 | 0.36234 |
| 244 k | chr19 | p13.3-p13.11 | 210395 | 20366351 | 20.2 | 0.856698 |
| 244 k | chr19 | q13.31-q13.33 | 37741966 | 61345316 | 23.6 | 0.381603 |
| 244 k | chr22 | q13.1-q13.2 | 14504218 | 41569277 | 27.1 | 0.327343 |
| 244 k | chrX | q25-q28 | 126061112 | 154570236 | 28.5 | 0.908502 |