Paediatric Chronic Myelogenous Leukaemia Presenting as B Cell Acute Lymphoblastic Leukaemia

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Introduction. Chronic myelogenous leukaemia (CML) is associated with BCR-ABL1 fusion gene formed by t(9;22) and located in Philadelphia (Ph) chromosome. The gene can produce 3 oncoproteins: p210 is found in > 90% of CML cases, p190 is usually associated with acute lymphoid leukaemia and p230 with chronic neutrophilic leukaemia. The tumour substrate consists of mature granulocytes, but t(9;22) is found in all myeloid cells and a part of lymphocytes. 3 CML phases have been identified: the most common chronic phase, followed by acceleration and blast crisis (BC) with > 20% blasts in blood/ marrow. The blasts are myeloid in 70% and lymphoid in 30% BC cases; active residual granulopoesis is usually preserved besides blast cells. BC is uncommon, occasional cases that initially present as CML-BC have been published. Paediatric CML is rare (2–3% leukaemias, 0.6–0.8 per million children per year).

Aim, material and methods. We report an unusual case of CML presenting initially as a lymphoblastic leukaemia in a child. The patient's clinical, laboratory, morphologic and genetic data from the archives of the Children's Clinical University Hospital's Departments of Hematooncology and Pathology were analysed.

Results. A 13–year-old boy was hospitalized in November, 2009 due to rapidly progressing fever, headaches, fatigue and hepatosplenomegaly. Blood test revealed WBC 510 × 10E9/l (blasts 82%, granulocytes 14% with left shift), HGB 8.5 g/dl, PLT 43 × 10E9/l. Total blast infiltration with residual hemopoesis < 5% was found on marrow cytology and trephine biopsy, blast cells were of B-precursor phenotype by flow cytometry and immunohistochemistry. Cytogenetic testing revealed Ph chromosome in all metaphases, BCR-ABL1 fusion (p210) was found. A rare unfavourable Ph-positive B-acute lymphoblastic leukaemia (B-ALL) was diagnosed and BFM-95 treatment protocol commenced. WBC dropped to 117 × 10E9/l with 7% blasts on day 2; cytomeric follow-up showed blood blasts < 10E-3 on day 8, marrow blasts on day 15 < 10E-3, no blasts on day 33. Granulocytes rapidly increased after induction (WBC up to 18 × 10E9/l, granulocytes 83% with shift till myelocytes, no blasts); unexpectedly, an increase of BCR-ABL1 transcript copies was simultaneously detected. Retrospectively, a possibility of primary CML-BC (lymphoblastic) was considered because of high granulocyte counts at admission and day 2 as well as p210 protein type. t(9;22) FISH was performed on blood cells, 95% segmented neutrophils and 53% mononuclear cells were positive, marking them as part of malignant clone. Thus, the diagnosis of CML was definitely proven. The patient was switched to CML-specific monotherapy with Imatinib – a specific BCR-ABL1 product inhibitor, achieved a complete molecular remission and is currently disease-free on therapy.

Conclusions. The patient presented was with several unusual features of CML, such as young age, initial presentation as lymphoid blast crisis, total reduction of myelopoesis in bone marrow, good response to therapy in spite of aggressive onset. The combination of these features seems to be unique; we have not found analogous cases published. The case illustrates both considerable diagnostic difficulties that could be faced in rare variants of well-known hematologic entities as well as the need for multipart and flexible diagnostic approach.