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HAEMATOLOGY CASE REPORT | December 2024

Haematologic malignancies

Acute myeloid leukaemia

Clinical information and laboratory results

A 70-year-old female patient was undergoing several courses of chemotherapy and radiation for non-small cell lung carcinoma. She presented at an outpatient clinic after developing malaise and markedly decreased exertion. Blood testing on an XR-Series analyser initially revealed anaemia (HGB = 8.2 g/dL, 5.1 mmol/L), thrombocytopenia (PLT = 44 × 10^3/µL), and slight leucocytosis (14.75 × 10^3/µL) (Fig. 1).

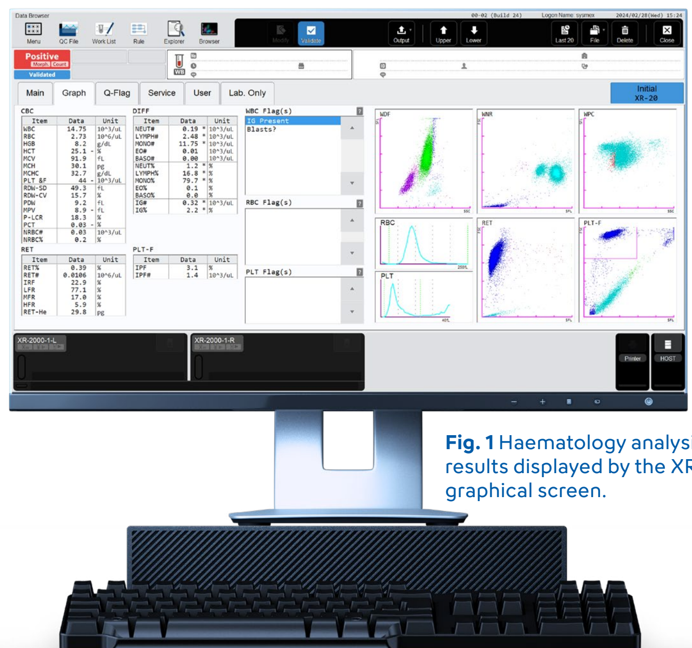

Fig. 1 Haematology analysis results displayed by the XR graphical screen.

The analyser triggered the flags 'IG Present' in the WDF channel and 'Blasts?' in the WPC channel. The respective WPC scattergram showed an increased presence of cells in the blast area (Fig. 2).

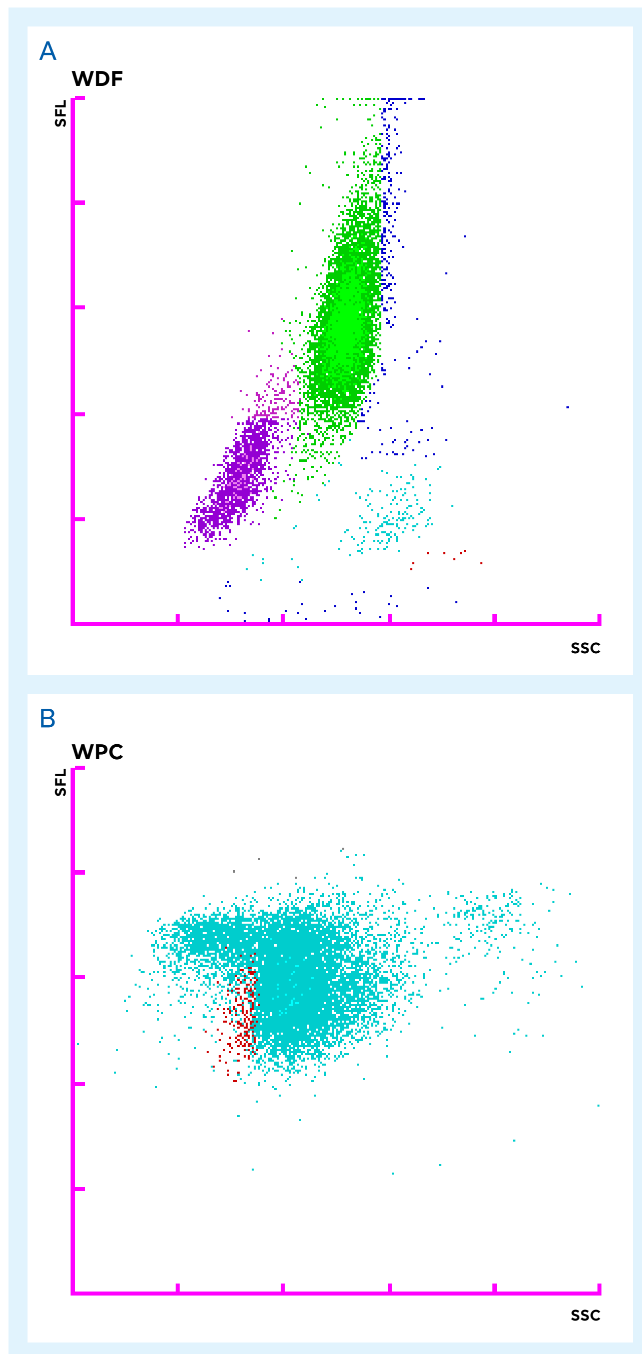

Fig. 2 The WDF scattergram showed presence of IG (blue dots, A) and the WPC scattergram showed presence of cells in the blast area of the scattergram (red dots, B).

Subsequently, a smear review was performed to review the cells' morphology revealing that 75% were blast cells. The subsequent immunophenotyping in the clinical flow laboratory confirmed the suspicion of acute myeloid leukaemia (AML).

Result interpretation

The classical CBC+DIFF analysis on Sysmex routine haematology analysers provides an initial indication for the presence of abnormal cells. This can be complemented by additional information gathered from the 'white precursor and pathological cell' (WPC) channel.

Differences in the staining mechanisms between the WDF and WPC channel reagents allow separating mature normal cells from precursor cells or malignant cells.

The membranes of white blood cells (WBC) are differently composed, depending on their maturity, function and activation status. The white blood cell differential (WDF) channel utilises a unique reagent combination that can separate WBC subtypes according to these differences in membrane composition and cytoplasmic content. The lysing reagent reacts rather gently, perforating the cell membrane and leaving the internal structure of the cells largely intact. This allows the fluorescence marker to enter the cell and label primarily RNA. Depending on the measurement signals of the cell clusters, i.e. fluorescence, forward- and side-scatter signals, specific flags are triggered, pre-classifying the sample as negative, reactive or potentially malignant. Based on this pre-classification in the WDF channel, the flag 'Blasts/Abn Lympho?' or the combination 'Blasts/Abn Lympho?' and 'Atypical Lympho?' can be triggered, leading to an automated reflex measurement in the WPC channel (Fig. 3).

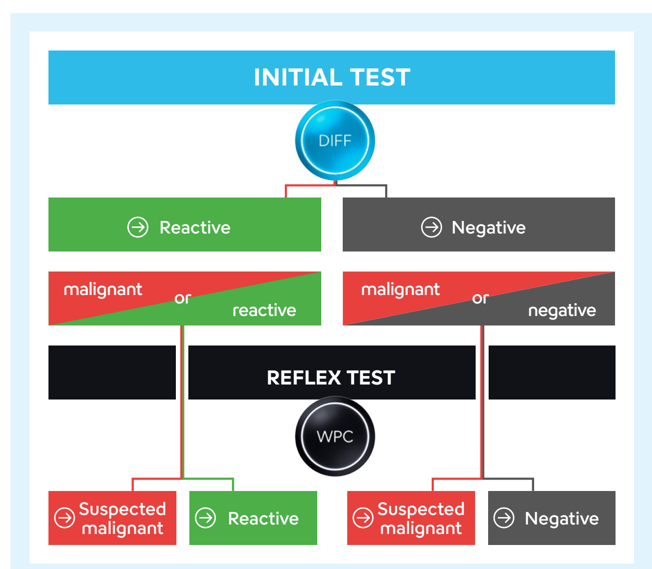

Fig. 3 Combining the DIFF and WPC analyses results in a dual-level approach to classify samples into three different, well-defined categories: negative, reactive (flag 'Atypical Lympho?') and suspected malignant (either flag 'Blasts?' and/or flag 'Abn Lympho?').

In comparison to the WDF channel, the lysis reagent of the WPC channel has a stronger impact on membrane lipids, resulting in a higher cell membrane permeability. With the polymethine concentration of the WPC fluorescence reagent being higher than that of the WDF channel, it labels DNA inside the nucleus instead of cytoplasmic RNA. The special characteristics of different WBC can be used for subpopulation differentiation, e.g. between abnormal lymphocytes and blast cells (Fig. 4).

In this example case, the flag 'IG Present' was triggered in the WDF channel. The immature granulocyte (IG) count includes promyelocytes, myelocytes and metamyelocytes. From the WPC channel, the flag 'Blasts?' was generated and the respective scattergram showed an increased presence of cells in the blast area. 'Blasts?' flags should be followed up since their presence could be indicative of the presence of acute malignancies. The WHO defined a cut-off for AML diagnosis that requires having at least 20% myeloid blasts in peripheral blood or bone marrow [1]. In this case, the subsequent immunophenotyping in the clinical flow laboratory confirmed the suspicion of AML.

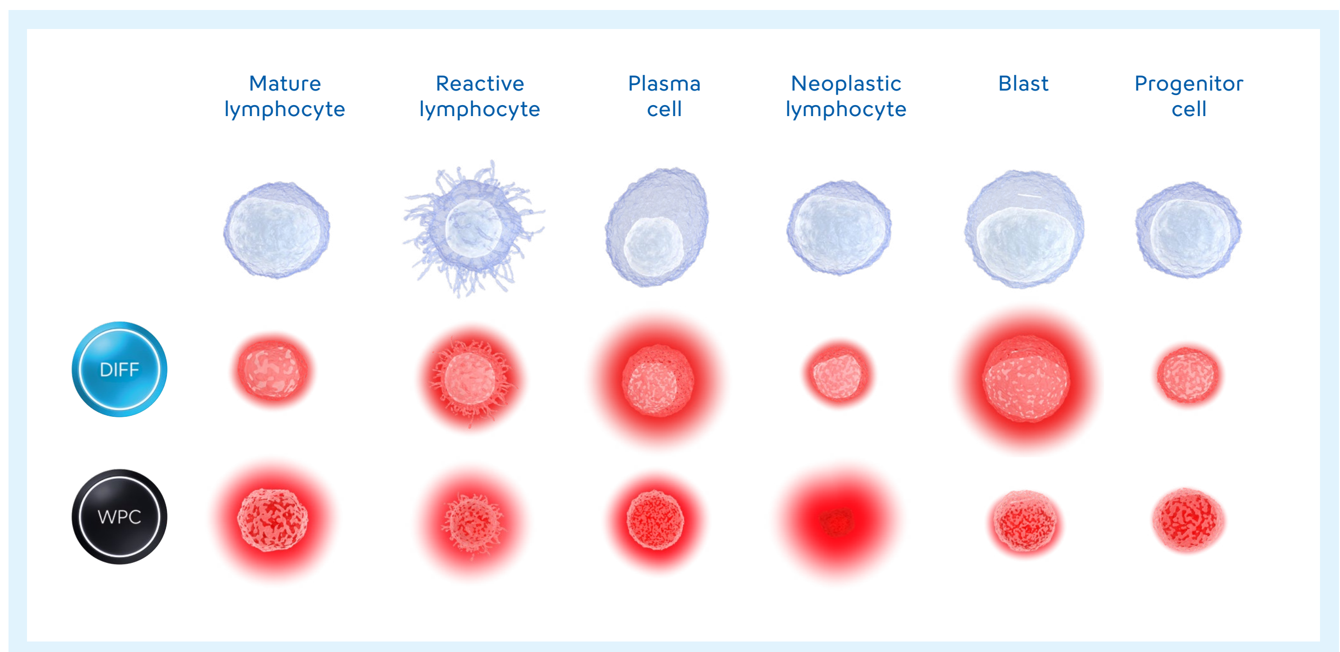

Fig. 4 Differences in the staining mechanisms between the WDF and WPC channel reagents allow separating mature normal lymphocytes from activated lymphocytes and precursor cells or malignant cells.

References

[1] **Khoury JD *et al.* (2022):** The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Myeloid and Histiocytic/Dendritic Neoplasms. Leukemia; 36(7), 1703–1719.