Aggressive Hematological Neoplasms Involving Plasmacytoid Dendritic Cells: A Three-Case Serie

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OBJECTIVE

Plasmacytoid Dendritic cell (pDC)-associated hematologic neoplasms represent a recently recognized entity with distinct and incompletely understood clinical presentations. This study examines three cases, highlighting the diversity and challenges in diagnosing and treating these neoplasms.

METHODS

We describe three clinical cases of pDC-associated neoplasms managed at the CHU of Liège, focusing on diagnostic challenges, genetic findings, and therapeutic strategies.

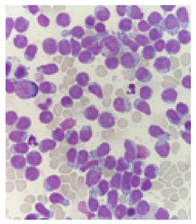
RESULTS

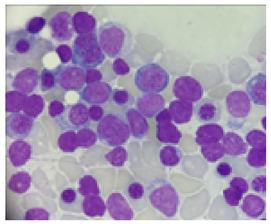
Case A : A 41-year-old woman underwent bone marrow (BM) biopsy following a skin biopsy suspicious for blastic plasmacytoid dendritic cell neoplasm (**BPDCN**). BM analysis revealed middle size blasts with peripheral nuclei and prominent pseudopodia. Immunophenotype (IPS) was CD123+, CD4+, CD56+, CD3−, CD19−,MPO, CD303-, CD304- but TCL1+, Optical genome mapping (OGM) identified multiple aberrations (t(2;9), t(6;16), partial 3p and 6q deletions), while next-generation sequencing (NGS) detected a *TET2* mutation. These findings confirmed a diagnosis of BPDCN. Initial treatment with tagraxofusp (**TAG**) achieved complete remission (CR), but relapse occurred after the third cycle. Combining TAG with azacitidine and venetoclax (**VenAZA**) induced a second CR.

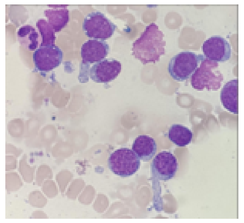
Case B : A 73-year-old man was evaluated for cytopenia after CAR-T cell for myeloma. Morphology and IPS revealed two clonal populations: myeloblasts (CD34+, CD45+, CD117heterogenous, CD123+, CD303-, CD304-, MPO−) and **immature pDCs** (**CD34+**, CD123+, CD4weak, CD303+, CD304+, CD56−, CD3−, CD19−). Sorting experiments enabled separate analyses of these populations using FISH, which uncovered **shared genetic alterations** (-7, +13). NGS identified *TET2* and *U2AF1* pathogenic/likely pathogenic (P/LP) mutations CNV. These findings supported a diagnosis of **pDC-AML**, given the genetic overlap commonly described in this scenario and the clonal expansion of pDCs. Due to dual CD123 expression and shared genomic alterations, we decided to treat the patient with **TAG** and obtained CR after cycle 1.

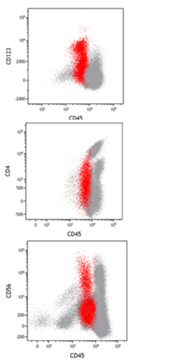
RESULTS

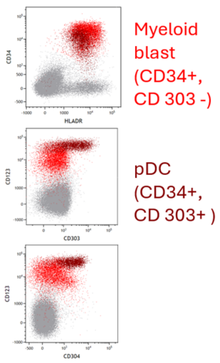
CASE A | CASE B | CASE C

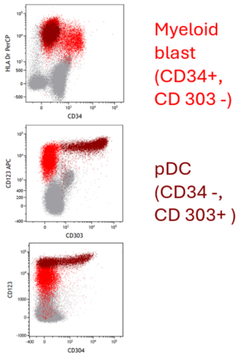


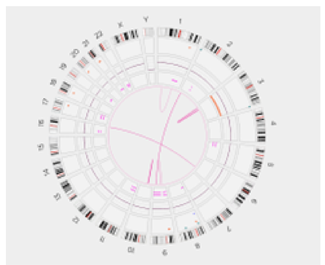


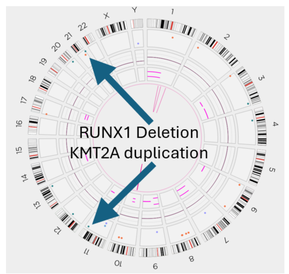




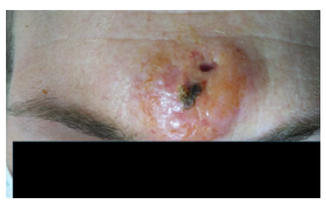




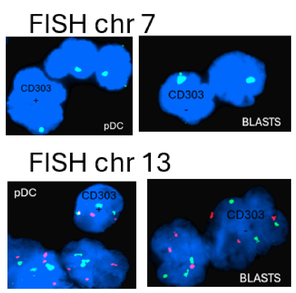


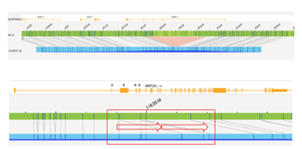


RUNX1 deletion



Clinical presentation at the diagnosis.





KMT2A duplication

RESULTS

Patient C : A 64-year-old man underwent BM exploration for cytopenia and skin lesions. Morphological examination revealed two abnormal clones: classic myeloblasts and a pDC population characterized by the presence of several thin pseudopodia. IPS identified two clonal populations: **myeloblasts** (CD34+, CD4low, CD56-, CD117+, CD123+, MPO−, CD303−, CD304−) and **mature pDCs** (CD34−, CD123bright, CD4+, CD56−, CD303+, CD304+). Genetic analysis detected *KMT2A* duplication, *RUNX1* deletion by OGM and multiple P/LP mutations (*FLT3, U2AF1, BCOR*) by NGS. The diagnosis was mature pDC-associated myeloid neoplasm (**MPDCP**) as we found a mature pDC population associated with a myeloid neoplasia. Treatment with **VenAZA** achieved CR1, but relapse occurred shortly thereafter.

CONCLUSION

These three cases highlight the complexity of neoplasms associated with **pDC**.

The WHO 5th edition defines **BPDCN** (case A) and **MPDCP** (case C) as distinct entities, but **pDC-AML** (case B), though mentioned, lacks clear classification and may be underdiagnosed without extensive knowledge in flow cytometry and genetics.

pDC-targeted therapies like tagraxofusp could offer promise for these patients, but further clarification and research are needed.

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