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Chemotherapy-Induced Bone Marrow Aplasia Associated with Hypoplastic Myelodysplastic Syndrome During Neoadjuvant Therapy for Inflammatory Breast Cancer: A Case Report and Literature Review

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Abstract | **Case Report**

Chemotherapy is a backbone treatmen in localized breast cancer but its non selective cytotoxic effect harms other body cells including the bone marrow blood cells precursors leading to pancytopenia but this is temporary and reversible. Chemotherapy induced bone marrow aplasia is a rare, potentially life-threatening complication and requires investigations to distinguish myelosuppression from irreversible therapy related bone marrow failure, hematologic disorders, or bone marrow infiltration. We report a case of chemotherapy induced bone marrow aplasia associated with hypoplastic myelodysplastic syndrome during neoadjuvant chemotherapy for synchronous bilateral breast cancer,which illustrates the diagnostic and therapeutic challenges posed by chemotherapy-induced bone marrow aplasia associated with hypoplastic myelodysplastic syndrome. Early hematologic evaluation, multidisciplinary collaboration, and supportive management may permit hematologic recovery and completion of curative treatment and even she had a complete pathological response but this did not eliminate the risk of early distant relapse, and this emphasizes the need for continued surveillance.

Keywords: Breast cancer; Bone marrow aplasia, Chemotherapy; Eltrombopag; Pathological complete response; Brain metastasis.

INTRODUCTION

Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer-related mortality among women worldwide. It mainly occurs in middle-aged and older women [2].

Neoadjuvant chemotherapy has become the standard of care for patients with locally advanced breast cancer and in cases where a conservation therapy is decided as the chemotherapy helps is size reduction. A lot of evidences are proved that the chemotherapy has an important role in improving tumor downstaging, surgical outcomes, and pathological complete response [pCR], which is associated with favorable long-term prognosis in aggressive breast cancer subtypes [3].

Neoadjuvant chemotherapy regimens are anthracycline and taxane-based therapy with or without platinum agents, remain the cornerstone of treatment for high-risk disease [4].

Although hematologic toxicity is a common adverse effect of cytotoxic chemotherapy, it is usually transient and manageable with supportive care or dose modifications. In contrast, severe chemotherapy-induced bone marrow aplasia is exceptionally rare in patients with solid tumors. Persistent cytopenias should prompt thorough evaluation to exclude bone marrow metastasis, therapy-related myeloid neoplasms, aplastic anemia, or other hematologic disorders [1]. Bone marrow aspiration, trephine biopsy, and cytogenetic studies are essential for establishing the diagnosis and guiding management [5].

PATIENT AND OBSERVATION

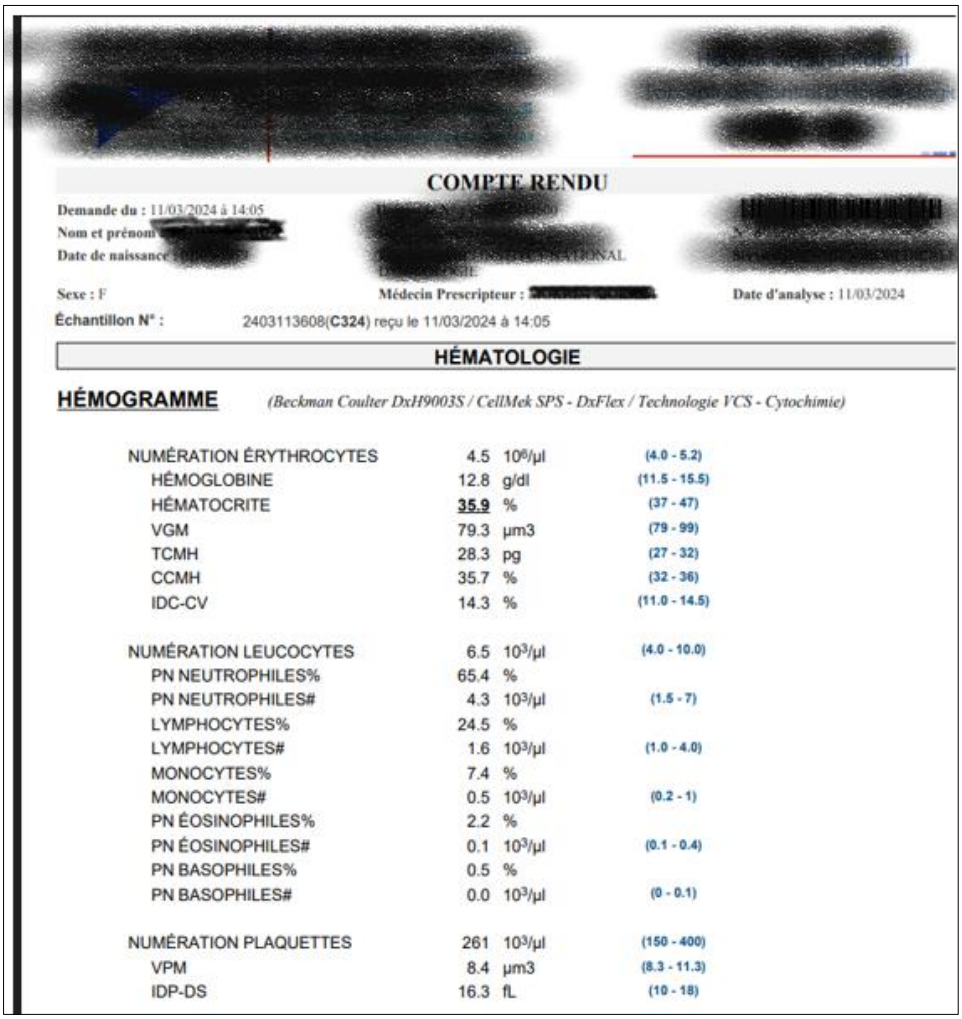
We report the case of a 47 years old premenopausal woman with no significant medical history and no family history of breast or ovarian cancer presented to our institution after noticing bilateral breast masses that had progressively increased in size over approximately one year. The delay in seeking medical

attention resulted in marked progression of the right breast lesion, which became inflammatory, whereas the left breast lesion remained localized. The patient had no previous history of hematologic disorders, autoimmune disease, chronic viral infection, or exposure to ionizing radiation or toxic chemicals. Her performance status at presentation was preserved, and she had no constitutional symptoms other than those related to the breast disease.

Physical examination revealed an inflammatory right breast mass associated with skin erythema, edema, nipple retraction, and palpable ipsilateral axillary lymphadenopathy. Examination of the left breast demonstrated a palpable lesion without inflammatory skin changes. No supraclavicular lymphadenopathy or evidence of distant metastatic disease was detected during the initial clinical evaluation.

In 13th of February 2023, bilateral mammography and echography were realized and revealed a multifocal right breast mass with lesions measuring 27x16,5 mm, 7x5,5 mm, 9,5x7,5 mm, 5x4 mm, and 9x6 mm; with axillairy lymphadenopathy measuring 13.5mm in the lowest axis, classified BIRADS 5. Microcalcification foci at the junctions of inferior quadrants classified BIRADS 4.

Core needle biopsies confirmed a right ductal carcinoma and a left intraductal carcinoma. Immunohistochemical analysis and staging investigations were performed and reveled a triple negative right breast cancer. The breast, and the case was discussed at the multidisciplinary breast tumor board. Given the locally advanced presentation, neoadjuvant dose dense chemotherapy of doxorubicine[100mg/m2] +cyclophosphamide 600 mg/m2 with granulocyte stimulating growth factor every two weeks followed by weekly palitaxe75mg/m2+carboplatin AUC2 were recommended andher initial CBC was normal [Fig.1].



COMPTE RENDU

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Nom et prénom :
Date de naissance :
Sexe : F
Médecin Prescripteur :
Date d'analyse : 11/03/2024
Échantillon N° : 2403113608(**C324**) reçu le 11/03/2024 à 14:05

HÉMATOLOGIE

HÉMOGRAMME *(Beckman Coulter DxH9003S / CellMek SPS - DxFlex / Technologie VCS - Cytochimie)*

NUMÉRATION ÉRYTHROCYTES	4.5	10^6/µl	(4.0 - 5.2)
HÉMOGLOBINE	12.8	g/dl	(11.5 - 15.5)
HÉMATOCRITE	**35.9**	%	(37 - 47)
VGM	79.3	µm3	(79 - 99)
TCMH	28.3	pg	(27 - 32)
CCMH	35.7	%	(32 - 36)
IDC-CV	14.3	%	(11.0 - 14.5)
NUMÉRATION LEUCOCYTES	6.5	10^3/µl	(4.0 - 10.0)
PN NEUTROPHILES%	65.4	%	
PN NEUTROPHILES#	4.3	10^3/µl	(1.5 - 7)
LYMPHOCYTES%	24.5	%	
LYMPHOCYTES#	1.6	10^3/µl	(1.0 - 4.0)
MONOCYTES%	7.4	%	
MONOCYTES#	0.5	10^3/µl	(0.2 - 1)
PN ÉOSINOPHILES%	2.2	%	
PN ÉOSINOPHILES#	0.1	10^3/µl	(0.1 - 0.4)
PN BASOPHILES%	0.5	%	
PN BASOPHILES#	0.0	10^3/µl	(0 - 0.1)
NUMÉRATION PLAQUETTES	261	10^3/µl	(150 - 400)
VPM	8.4	µm3	(8.3 - 11.3)
IDP-DS	16.3	fL	(10 - 18)

Figure 1

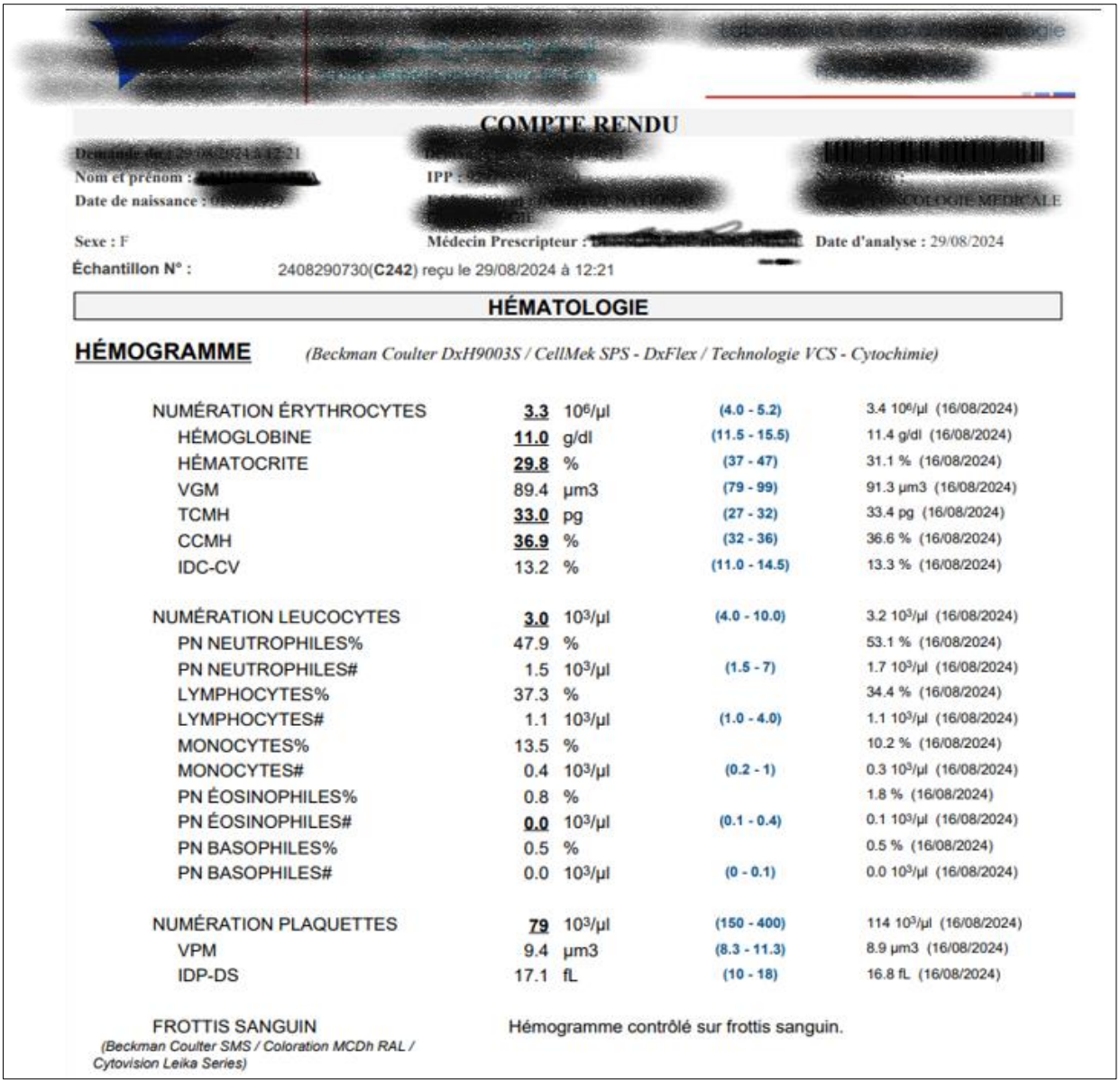
During treatment by paclitaxel and carboplatin, she developed grade III neutropenia requiring supportive management. Although neutrophil counts subsequently recovered, persistent thrombocytopenia developed and progressively worsened despite treatment interruption.

Serial platelet counts demonstrated persistent thrombocytopenia, decreasing from 79 × 10^9/L on 29 August 2024[Fig.2] to 31 × 10^9/L on 5 September 2024 [Fig.3], with only partial recovery to 41 × 10^9/L on 24 September 2024[Fig.4]. The persistence and severity of thrombocytopenia were considered disproportionate to expected chemotherapy-induced myelosuppression, prompting referral to the hematology department for further evaluation.

Bone marrow trephine biopsy demonstrated marked bone marrow hypocellularity without evidence of metastatic breast cancer infiltration. Bone marrow aspiration [myelogram] showed dysplastic hematopoietic changes interpreted by the hematologist as hypoplastic myelodysplastic syndrome, while conventional cytogenetic analysis revealed a normal female karyotype. These findings excluded bone marrow metastasis and supported the diagnosis of chemotherapy-induced bone marrow aplasia associated with hypoplastic myelodysplastic syndrome.

Following multidisciplinary discussion cytotoxic chemotherapy was discontinued because of severe and persistent bone marrow toxicity.

The patient was started on eltrombopag [Revolade®] at a dose of 50 mg once daily. After one month of treatment, the platelet count increased to 44 × 10^9/L [Fig.5], which was considered insufficient for definitive surgical management. Consequently, the eltrombopag dose was increased to 75 mg once daily on 2 January 2025, resulting in progressive hematologic recovery that allowed surgical treatment as shown in Fig.6.



COMPTE RENDU

Nom et prénom : [redacted] IPP : [redacted]

Date de naissance : [redacted]

Sexe : F Médecin Prescripteur : [redacted] Date d'analyse : 29/08/2024

Échantillon N° : 2408290730(**C242**) reçu le 29/08/2024 à 12:21

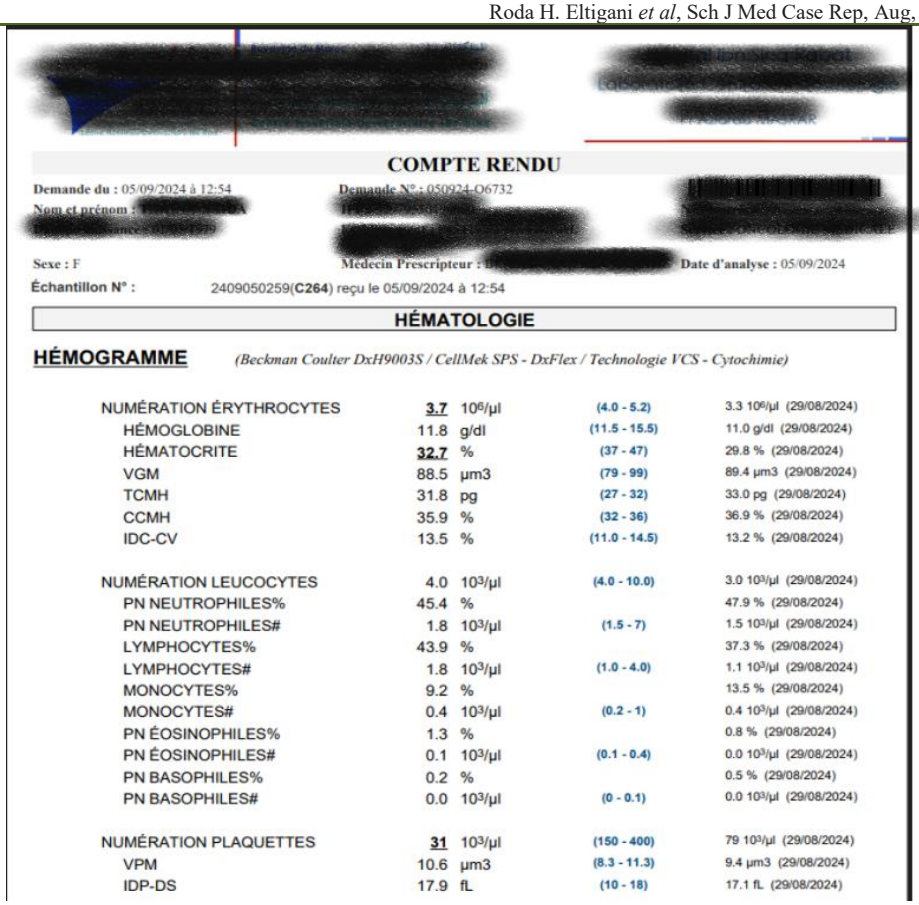
HÉMATOLOGIE

HÉMOGRAMME *(Beckman Coulter DxH9003S / CellMek SPS - DxFlex / Technologie VCS - Cytochimie)*

NUMÉRATION ÉRYTHROCYTES	**3.3**	10^6/µl	(4.0 - 5.2)	3.4 10^6/µl (16/08/2024)
HÉMOGLOBINE	**11.0**	g/dl	(11.5 - 15.5)	11.4 g/dl (16/08/2024)
HÉMATOCRITE	**29.8**	%	(37 - 47)	31.1 % (16/08/2024)
VGM	89.4	µm3	(79 - 99)	91.3 µm3 (16/08/2024)
TCMH	**33.0**	pg	(27 - 32)	33.4 pg (16/08/2024)
CCMH	**36.9**	%	(32 - 36)	36.6 % (16/08/2024)
IDC-CV	13.2	%	(11.0 - 14.5)	13.3 % (16/08/2024)
NUMÉRATION LEUCOCYTES	**3.0**	10^3/µl	(4.0 - 10.0)	3.2 10^3/µl (16/08/2024)
PN NEUTROPHILES%	47.9	%		53.1 % (16/08/2024)
PN NEUTROPHILES#	1.5	10^3/µl	(1.5 - 7)	1.7 10^3/µl (16/08/2024)
LYMPHOCYTES%	37.3	%		34.4 % (16/08/2024)
LYMPHOCYTES#	1.1	10^3/µl	(1.0 - 4.0)	1.1 10^3/µl (16/08/2024)
MONOCYTES%	13.5	%		10.2 % (16/08/2024)
MONOCYTES#	0.4	10^3/µl	(0.2 - 1)	0.3 10^3/µl (16/08/2024)
PN ÉOSINOPHILES%	0.8	%		1.8 % (16/08/2024)
PN ÉOSINOPHILES#	**0.0**	10^3/µl	(0.1 - 0.4)	0.1 10^3/µl (16/08/2024)
PN BASOPHILES%	0.5	%		0.5 % (16/08/2024)
PN BASOPHILES#	0.0	10^3/µl	(0 - 0.1)	0.0 10^3/µl (16/08/2024)
NUMÉRATION PLAQUETTES	**79**	10^3/µl	(150 - 400)	114 10^3/µl (16/08/2024)
VPM	9.4	µm3	(8.3 - 11.3)	8.9 µm3 (16/08/2024)
IDP-DS	17.1	fL	(10 - 18)	16.8 fL (16/08/2024)

FROTTIS SANGUIN *(Beckman Coulter SMS / Coloration MCDh RAL / Cytovision Leika Series)* Hémogramme contrôlé sur frottis sanguin.

Figure 2



COMPTE RENDU

Demande du : 05/09/2024 à 12:54 Demande N° : 050924-O6732

Nom et prénom :

Sexe : F Médecin Prescripteur : Date d'analyse : 05/09/2024

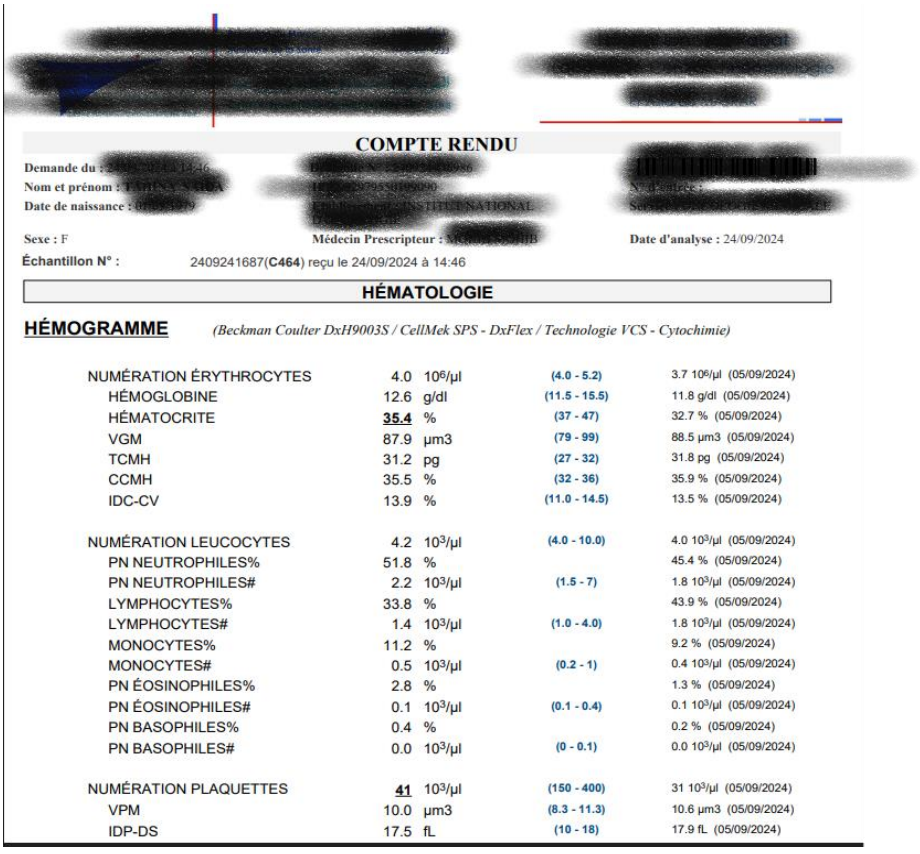
Échantillon N° : 2409050259(**C264**) reçu le 05/09/2024 à 12:54

HÉMATOLOGIE

HÉMOGRAMME *(Beckman Coulter DxH9003S / CellMek SPS - DxFlex / Technologie VCS - Cytochimie)*

NUMÉRATION ÉRYTHROCYTES	**3.7**	10^6/µl	(4.0 - 5.2)	3.3 10^6/µl (29/08/2024)
HÉMOGLOBINE	11.8	g/dl	(11.5 - 15.5)	11.0 g/dl (29/08/2024)
HÉMATOCRITE	**32.7**	%	(37 - 47)	29.8 % (29/08/2024)
VGM	88.5	µm3	(79 - 99)	89.4 µm3 (29/08/2024)
TCMH	31.8	pg	(27 - 32)	33.0 pg (29/08/2024)
CCMH	35.9	%	(32 - 36)	36.9 % (29/08/2024)
IDC-CV	13.5	%	(11.0 - 14.5)	13.2 % (29/08/2024)
NUMÉRATION LEUCOCYTES	4.0	10^3/µl	(4.0 - 10.0)	3.0 10^3/µl (29/08/2024)
PN NEUTROPHILES%	45.4	%		47.9 % (29/08/2024)
PN NEUTROPHILES#	1.8	10^3/µl	(1.5 - 7)	1.5 10^3/µl (29/08/2024)
LYMPHOCYTES%	43.9	%		37.3 % (29/08/2024)
LYMPHOCYTES#	1.8	10^3/µl	(1.0 - 4.0)	1.1 10^3/µl (29/08/2024)
MONOCYTES%	9.2	%		13.5 % (29/08/2024)
MONOCYTES#	0.4	10^3/µl	(0.2 - 1)	0.4 10^3/µl (29/08/2024)
PN ÉOSINOPHILES%	1.3	%		0.8 % (29/08/2024)
PN ÉOSINOPHILES#	0.1	10^3/µl	(0.1 - 0.4)	0.0 10^3/µl (29/08/2024)
PN BASOPHILES%	0.2	%		0.5 % (29/08/2024)
PN BASOPHILES#	0.0	10^3/µl	(0 - 0.1)	0.0 10^3/µl (29/08/2024)
NUMÉRATION PLAQUETTES	**31**	10^3/µl	(150 - 400)	79 10^3/µl (29/08/2024)
VPM	10.6	µm3	(8.3 - 11.3)	9.4 µm3 (29/08/2024)
IDP-DS	17.9	fL	(10 - 18)	17.1 fL (29/08/2024)

Figure 3



COMPTE RENDU

Demande du :

Nom et prénom :

Date de naissance :

Sexe : F Médecin Prescripteur : Date d'analyse : 24/09/2024

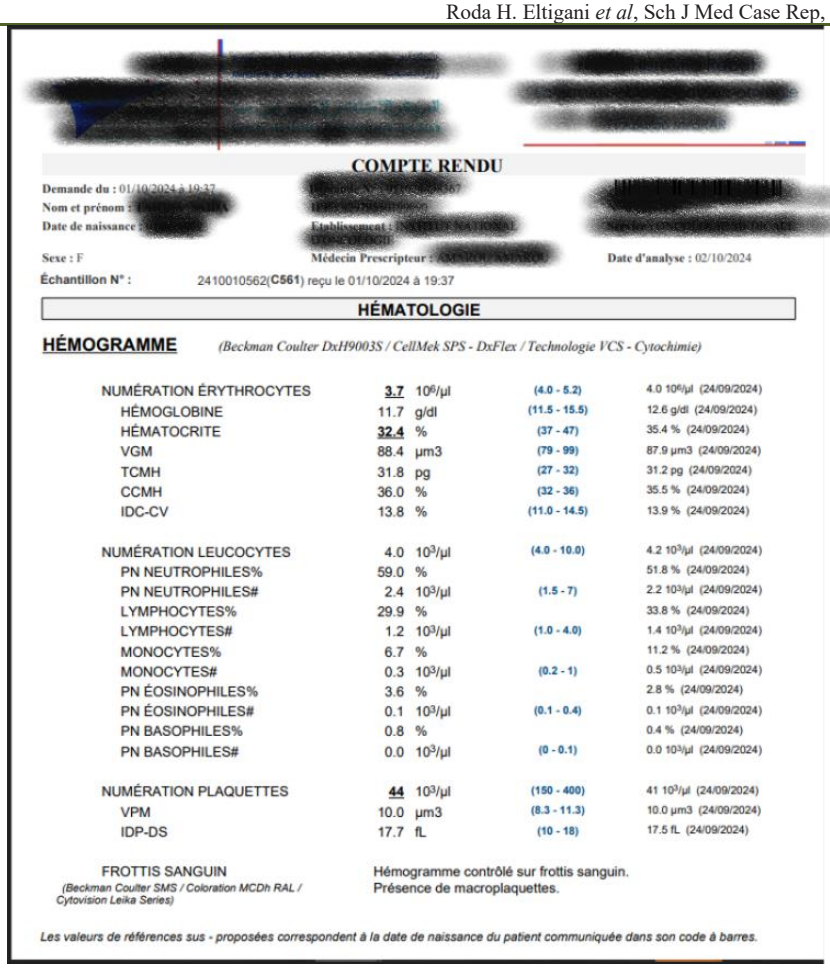
Échantillon N° : 2409241687(**C464**) reçu le 24/09/2024 à 14:46

HÉMATOLOGIE

HÉMOGRAMME *(Beckman Coulter DxH9003S / CellMek SPS - DxFlex / Technologie VCS - Cytochimie)*

NUMÉRATION ÉRYTHROCYTES	4.0	10^6/µl	(4.0 - 5.2)	3.7 10^6/µl (05/09/2024)
HÉMOGLOBINE	12.6	g/dl	(11.5 - 15.5)	11.8 g/dl (05/09/2024)
HÉMATOCRITE	**35.4**	%	(37 - 47)	32.7 % (05/09/2024)
VGM	87.9	µm3	(79 - 99)	88.5 µm3 (05/09/2024)
TCMH	31.2	pg	(27 - 32)	31.8 pg (05/09/2024)
CCMH	35.5	%	(32 - 36)	35.9 % (05/09/2024)
IDC-CV	13.9	%	(11.0 - 14.5)	13.5 % (05/09/2024)
NUMÉRATION LEUCOCYTES	4.2	10^3/µl	(4.0 - 10.0)	4.0 10^3/µl (05/09/2024)
PN NEUTROPHILES%	51.8	%		45.4 % (05/09/2024)
PN NEUTROPHILES#	2.2	10^3/µl	(1.5 - 7)	1.8 10^3/µl (05/09/2024)
LYMPHOCYTES%	33.8	%		43.9 % (05/09/2024)
LYMPHOCYTES#	1.4	10^3/µl	(1.0 - 4.0)	1.8 10^3/µl (05/09/2024)
MONOCYTES%	11.2	%		9.2 % (05/09/2024)
MONOCYTES#	0.5	10^3/µl	(0.2 - 1)	0.4 10^3/µl (05/09/2024)
PN ÉOSINOPHILES%	2.8	%		1.3 % (05/09/2024)
PN ÉOSINOPHILES#	0.1	10^3/µl	(0.1 - 0.4)	0.1 10^3/µl (05/09/2024)
PN BASOPHILES%	0.4	%		0.2 % (05/09/2024)
PN BASOPHILES#	0.0	10^3/µl	(0 - 0.1)	0.0 10^3/µl (05/09/2024)
NUMÉRATION PLAQUETTES	**41**	10^3/µl	(150 - 400)	31 10^3/µl (05/09/2024)
VPM	10.0	µm3	(8.3 - 11.3)	10.6 µm3 (05/09/2024)
IDP-DS	17.5	fL	(10 - 18)	17.9 fL (05/09/2024)

Figure 4



COMPTE RENDU

Demande du : 01/10/2024 à 19:37
Nom et prénom :
Date de naissance :
Etablissement :
Sexe : F
Médecin Prescripteur :
Date d'analyse : 02/10/2024
Échantillon N° : 2410010562(**C561**) reçu le 01/10/2024 à 19:37

HÉMATOLOGIE

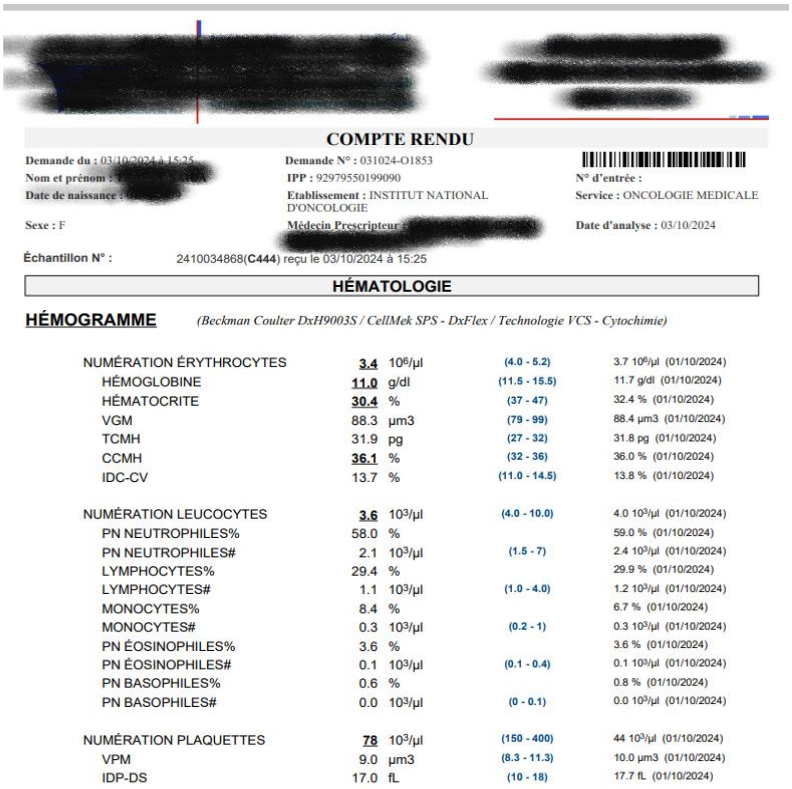
HÉMOGRAMME *(Beckman Coulter DxH9003S / CellMek SPS - DxFlex / Technologie VCS - Cytochimie)*

NUMÉRATION ÉRYTHROCYTES	**3.7**	10^6/µl	(4.0 - 5.2)	4.0 10^6/µl (24/09/2024)
HÉMOGLOBINE	11.7	g/dl	(11.5 - 15.5)	12.6 g/dl (24/09/2024)
HÉMATOCRITE	**32.4**	%	(37 - 47)	35.4 % (24/09/2024)
VGM	88.4	µm3	(79 - 99)	87.9 µm3 (24/09/2024)
TCMH	31.8	pg	(27 - 32)	31.2 pg (24/09/2024)
CCMH	36.0	%	(32 - 36)	35.5 % (24/09/2024)
IDC-CV	13.8	%	(11.0 - 14.5)	13.9 % (24/09/2024)
NUMÉRATION LEUCOCYTES	4.0	10^3/µl	(4.0 - 10.0)	4.2 10^3/µl (24/09/2024)
PN NEUTROPHILES%	59.0	%		51.8 % (24/09/2024)
PN NEUTROPHILES#	2.4	10^3/µl	(1.5 - 7)	2.2 10^3/µl (24/09/2024)
LYMPHOCYTES%	29.9	%		33.8 % (24/09/2024)
LYMPHOCYTES#	1.2	10^3/µl	(1.0 - 4.0)	1.4 10^3/µl (24/09/2024)
MONOCYTES%	6.7	%		11.2 % (24/09/2024)
MONOCYTES#	0.3	10^3/µl	(0.2 - 1)	0.5 10^3/µl (24/09/2024)
PN ÉOSINOPHILES%	3.6	%		2.8 % (24/09/2024)
PN ÉOSINOPHILES#	0.1	10^3/µl	(0.1 - 0.4)	0.1 10^3/µl (24/09/2024)
PN BASOPHILES%	0.8	%		0.4 % (24/09/2024)
PN BASOPHILES#	0.0	10^3/µl	(0 - 0.1)	0.0 10^3/µl (24/09/2024)
NUMÉRATION PLAQUETTES	**44**	10^3/µl	(150 - 400)	41 10^3/µl (24/09/2024)
VPM	10.0	µm3	(8.3 - 11.3)	10.0 µm3 (24/09/2024)
IDP-DS	17.7	fL	(10 - 18)	17.5 fL (24/09/2024)

FROTTIS SANGUIN *(Beckman Coulter SMS / Coloration MCDh RAL / Cytovision Leika Series)* — Hémogramme contrôlé sur frottis sanguin. Présence de macroplaquettes.

Les valeurs de références sus - proposées correspondent à la date de naissance du patient communiquée dans son code à barres.

Figure 5



COMPTE RENDU

Demande du : 03/10/2024 à 15:25
Demande N° : 031024-O1853
IPP : 92979550199090
N° d'entrée :
Nom et prénom :
Date de naissance :
Etablissement : INSTITUT NATIONAL D'ONCOLOGIE
Service : ONCOLOGIE MEDICALE
Sexe : F
Médecin Prescripteur :
Date d'analyse : 03/10/2024
Échantillon N° : 2410034868(**C444**) reçu le 03/10/2024 à 15:25

HÉMATOLOGIE

HÉMOGRAMME *(Beckman Coulter DxH9003S / CellMek SPS - DxFlex / Technologie VCS - Cytochimie)*

NUMÉRATION ÉRYTHROCYTES	**3.4**	10^6/µl	(4.0 - 5.2)	3.7 10^6/µl (01/10/2024)
HÉMOGLOBINE	**11.0**	g/dl	(11.5 - 15.5)	11.7 g/dl (01/10/2024)
HÉMATOCRITE	**30.4**	%	(37 - 47)	32.4 % (01/10/2024)
VGM	88.3	µm3	(79 - 99)	88.4 µm3 (01/10/2024)
TCMH	31.9	pg	(27 - 32)	31.8 pg (01/10/2024)
CCMH	**36.1**	%	(32 - 36)	36.0 % (01/10/2024)
IDC-CV	13.7	%	(11.0 - 14.5)	13.8 % (01/10/2024)
NUMÉRATION LEUCOCYTES	**3.6**	10^3/µl	(4.0 - 10.0)	4.0 10^3/µl (01/10/2024)
PN NEUTROPHILES%	58.0	%		59.0 % (01/10/2024)
PN NEUTROPHILES#	2.1	10^3/µl	(1.5 - 7)	2.4 10^3/µl (01/10/2024)
LYMPHOCYTES%	29.4	%		29.9 % (01/10/2024)
LYMPHOCYTES#	1.1	10^3/µl	(1.0 - 4.0)	1.2 10^3/µl (01/10/2024)
MONOCYTES%	8.4	%		6.7 % (01/10/2024)
MONOCYTES#	0.3	10^3/µl	(0.2 - 1)	0.3 10^3/µl (01/10/2024)
PN ÉOSINOPHILES%	3.6	%		3.6 % (01/10/2024)
PN ÉOSINOPHILES#	0.1	10^3/µl	(0.1 - 0.4)	0.1 10^3/µl (01/10/2024)
PN BASOPHILES%	0.6	%		0.8 % (01/10/2024)
PN BASOPHILES#	0.0	10^3/µl	(0 - 0.1)	0.0 10^3/µl (01/10/2024)
NUMÉRATION PLAQUETTES	**78**	10^3/µl	(150 - 400)	44 10^3/µl (01/10/2024)
VPM	9.0	µm3	(8.3 - 11.3)	10.0 µm3 (01/10/2024)
IDP-DS	17.0	fL	(10 - 18)	17.7 fL (01/10/2024)

Figure: 6

On 7 March 2025, the patient underwent right total mastectomy with axillary lymph node dissection and left total mastectomy with sentinel lymph node biopsy.

Histopathological examination of the right breast demonstrated:

- Absence of residual invasive carcinoma.
- Fibrocystic breast disease without atypia.
- No lymphovascular invasion.
- Tumor-free surgical margins.
- No metastatic involvement of the dissected axillary lymph nodes [**0/17**], with evidence of treatment-related regression.

The pathological response was classified as Sataloff TA/NA and Chevallier Grade 1, consistent with a pathological complete response of the invasive carcinoma.

Histopathological examination of the left breast revealed non-atypical fibrocystic changes without residual invasive carcinoma. Surgical margins were free of tumor. Sentinel lymph node biopsy demonstrated no metastatic involvement [0/4 lymph nodes].

Following surgery, the patient received adjuvant hypofractionated radiotherapy according to institutional practice.

The immediate postoperative course was uneventful, and hematologic parameters remained sufficiently stable under continued hematology follow-up.

Approximately four months after surgery, the patient developed neurological symptoms. Brain magnetic resonance imaging performed on 2 September 2025 demonstrated a solitary left frontoparietal intra-axial lesion measuring 28 × 27 mm with significant mass effect, highly suggestive of a metastatic brain lesion.

The patient was subsequently discussed during the multidisciplinary tumor board meeting to determine the most appropriate therapeutic strategy, taking into consideration the isolated nature of the intracranial relapse, her previous severe hematologic toxicity, and her overall clinical condition and the decision was to operate the patient then to start a sterotactic radiotherapy of the tumor bed then to demand BRC1/2 mutations and starting a 1st line chemotherapy of of: Gemcitabine-Carboplatin meanwhile.

DISCUSSION

Chemotherapy-induced bone marrow aplasia is an exceptionally uncommon but potentially life-threatening complication in patients receiving systemic treatment for solid malignancies. While transient myelosuppression is an anticipated consequence of cytotoxic chemotherapy, prolonged pancytopenia or isolated severe thrombocytopenia that persists despite treatment interruption should prompt investigation for alternative etiologies, including bone marrow metastasis, therapy-related myeloid neoplasms, aplastic anemia, nutritional deficiencies, viral infections, and immune-mediated cytopenias [6]. The carboplatin is one of the most frequent chemotherapy agents which cause a permanent bone morrow injury and hence bone marrow aplasia [7]. In such circumstances, early hematologic assessment with bone marrow aspiration and trephine biopsy is essential to establish the diagnosis and guide subsequent management [5].

The patient described in this report developed persistent thrombocytopenia during neoadjuvant chemotherapy consisting of dose-dense doxorubicin and cyclophosphamide followed by weekly paclitaxel and carboplatin. Although hematologic toxicity is frequently encountered with these agents, prolonged bone marrow failure requiring discontinuation of potentially curative treatment remains distinctly uncommon.

Doxorubicin associated with cyclophosphamide followed by paclitaxel have been reported to exert marked bone marrow toxic effects, with paclitaxel particularly impairing bone marrow recovery [8].

The persistence of severe thrombocytopenia in our patient, despite appropriate supportive measures, raised concern for an underlying bone marrow disorder rather than uncomplicated chemotherapy-induced myelosuppression.

Bone marrow biopsy demonstrated marked hypocellularity without evidence of metastatic breast cancer infiltration, thereby excluding one of the most important differential diagnoses in patients with advanced breast cancer and persistent cytopenias. Bone marrow aspiration performed by the hematology team demonstrated dysplastic hematopoietic changes consistent with hypoplastic myelodysplastic syndrome, while conventional cytogenetic analysis revealed a normal female karyotype. Distinguishing hypoplastic myelodysplastic syndrome from severe chemotherapy-induced marrow injury and aplastic anemia is challenging because these entities share several clinical and pathological characteristics, including hypocellular marrow and peripheral cytopenias [9]. In our patient, the diagnosis was established by the hematologist based on the integrated interpretation of marrow morphology and cytogenetic findings. Although classical therapy-related myelodysplastic syndrome usually develops several years after exposure to cytotoxic chemotherapy [10], this unusually early presentation suggests that chemotherapy may have unmasked a previously silent clonal hematopoietic disorder or induced profound marrow injury with dysplastic features. Regardless of the precise mechanism, recognition of this complication was

essential because it directly influenced subsequent therapeutic decisions.

Management of chemotherapy-induced bone marrow aplasia has not been standardized because of its rarity. Treatment generally consists of immediate discontinuation of the offending chemotherapy, intensive supportive care, transfusion support when required, infection prevention, and close collaboration between oncologists and hematologists. Eltrombopag, an oral thrombopoietin receptor agonist, has demonstrated efficacy in severe aplastic anemia and has increasingly been investigated for chemotherapy-induced thrombocytopenia [11].

CONCLUSION

Severe chemotherapy-induced bone marrow aplasia associated with hypoplastic myelodysplastic syndrome is an exceptionally rare complication during neoadjuvant treatment for breast cancer. This case illustrates the importance of recognizing persistent cytopenias that are disproportionate to expected chemotherapy-induced myelosuppression and emphasizes the need for early hematologic evaluation, including bone marrow aspiration and biopsy, to exclude marrow infiltration and other hematologic disorders. Multidisciplinary collaboration enabled prompt diagnosis, discontinuation of cytotoxic chemotherapy, and successful treatment with eltrombopag, allowing definitive surgery despite prolonged thrombocytopenia.

This report also demonstrates that pathological complete response may be achieved despite premature discontinuation of neoadjuvant chemotherapy. Nevertheless, the subsequent development of an isolated brain metastasis highlights that pathological complete response does not necessarily eradicate occult micrometastatic disease and should not replace careful post-treatment surveillance. Reporting similar cases may improve recognition of this rare complication and contribute to the development of evidence-based management strategies.

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