Characteristics and outcome of breast cancer-related microangiopathic haemolytic anaemia: a multicenter study

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Background

Cancer-related microangiopathic haemolytic anemia (MAHA) is a rare but life-threatening paraneoplastic syndrome first described in 1979 (1). Only single cases or small series with mixed cancer types have been reported so far (2). We conducted the first multicenter retrospective study focused on breast cancer related-MAHA (BC-MAHA) characteristics, outcomes, and prognostic factors

Methods

13 centers in France were contacted for this retrospective study of patients treated for BC over the past 20 years. Presence of schistocytes and either low haptoglobin or cytopenia was mandatory for retaining diagnosis of MAHA. Patients with MAHA from other causes than BC were excluded, as well as patients treated with gemcitabine or bevacizumab prior to MAHA diagnosis. Patient characteristics, treatments and outcome were retrieved from digital medical records. Overall survival (OS) was measured from the date of MAHA diagnosis until the date of death or last follow-up date.

Results

Table 1: Primary Tumor characteristics (N = 54).

	Patients	
Characteristic	N	%
Histological type		
IC-NST	29	55.8
mixed with lobular component + ILC	23	44.2
Others	2	
Histological grade		
I-II	39	75
III	13	25
NA	2	
Primary tumor size		
T1-2	32	61.5
T3-4	20	38.5
NA	2	
Nodal status		
N0	14	26.9
N+	38	73.1
NA	2	
IHC profile		
ER-/PR-/HER2-	8	16.7
HER2+	7	14.6
ER+/PR+/HER2-	33	68.8

On individual data from 54 patients with BC-MAHA obtained, 23 patients (44%) had a lobular BC and most BC were low grade (gradeI/II, N=39, 75%)

Table 2: Clinical and biological characteristics at MAHA diagnosis (N = 54).

	Patients	
Characteristic	N	%
PS		
PS 1-2	30	55.6
PS 3-4	24	44.4
Metastasis		
Bone marrow	14	25.9
Bone	44	81.5
Lung	8	14.8
Liver	35	64.8
Others	32	59.3
Platelets		
<50G/L	29	53.7
≥50G/L	25	46.3
Hemoglobin		
<8g/dL	26	48.1
≥8g/dL	28	51.9
Schistocytes		
≤5%	30	75
>5%	10	25
NA	17	
Circulating erythroblasts	40	85.1
Circulating myelemia	38	90.5
Prothrombin time		
<50%	8	16
≥50%	42	84
Glomerular Filtration Rate		
<30ml/min	4	10.5
30-60ml/min	9	23.7
>60ml/min	25	65.8
NA	16	
Total Bilirubin Level		
<1.24mg/dL	36	69.2
≥1.24mg/dL	36	69.2

Median overall survival was 28 days

(range: 0-1035; Q110, Q3:186)

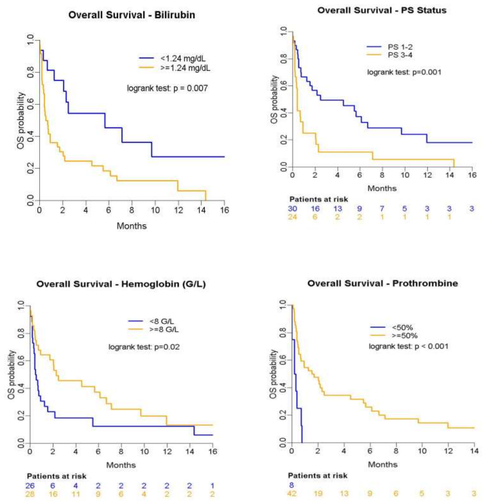
Table 3: prognostic factors associated with survival at 4 weeks (univariate analysis)

Factors	Categories	OR	95%CI	*P* value
PS at MAHA diagnosis	PS 1-2 PS 3-4	1.0 6.0	[1.8: 19.8]	0.002
Haemoglobin level	< 8g/dL **≥ 8g/dL**	1.0 4.0	[1.3; 12.0]	0.013
Total Bilirubin level	< 1.24mg/dL **≥ 1.24mg/dL**	1.0 5.5	[1.5; 20.6]	0.01
Prothrombin Time	< 50% **≥ 50%**	1.0 7.1	[0.9;50.0]	0.03
Time between first metastasis and MAHA	<16 months **≥ 16 months**	1.0 4.8	[1.5; 15.0]	0.01

Table 4: prognostic factors associated with survival at 4 weeks (multivariate analysis)

Factors	Categories	OR	95%CI	*P* value
PS at MAHA diagnosis	PS 1-2 PS 3-4	1.0 6.1	[1.4: 25.9]	0.01
Haemoglobin level	< 8g/dL **≥ 8g/dL**	1.0 4.0	[1.0; 16.7]	0.06
Total Bilirubin level	< 1.24mg/dL **≥ 1.24mg/dL**	1.0 4.7	[1.0; 24.0]	0.04
Prothrombin time	< 50% **≥ 50%**	1.0 11.1	[1.1; 100.0]	0.03

Figure 2: Kaplan Meyer estimates of overall survival – prognosis factors associated with survival at 4 weeks (multivariate analysis)



PS 3-4, elevated bilirubin, haemoglobin <80g/dL and prothrombin time <50% were significantly associated with a higher risk of death within four weeks of MAHA diagnosis

Conclusions

This study is the first attempt at characterizing BC-MAHA, which appears to be more frequent in the lobular subtype. In spite of a dismal median OS, a few patients experienced long survival and we document, for the first-time, prognostic factors that may guide therapeutic decision making.

REFERENCES

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