

## Leukemoid Reaction: Presentation of Two Cases

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The leukemoid reaction is defined by the presence in peripheral blood of white cells above 50,000/mm<sup>3</sup> or neutrophils above 30,000/mm<sup>3</sup>. The frequency varies between 1.3 and 15% of newborns admitted to neonatal intensive care units [1]. It usually appears during the first two weeks of life and more frequently during the first four days, the duration is about 8.5 days [2]. In extremely premature, this process is produced by an inflammatory response that active cytokines who increased granulocyte colony-stimulating factors (G-CSF). These induce the production of neutrophils that cause hyperleukocytosis.

These cytokines are produced in diseases related with prematurity such as brain white matter injury, respiratory failure with progression to bronchopulmonary dysplasia or necrotizing enterocolitis. The leukemoid reaction is also associated with the administration of neonatal steroids, infections, severe anemia and bronchopulmonary dysplasia [2,3].

### Case 1

A 28-week gestational female newborn admitted to the neonatal intensive care unit for extreme prematurity and respiratory distress. It was the fifth gestation of a 36 years old woman. She had pregestational diabetes mellitus treated with insulin, morbid obesity, arterial hypertension and

polycystic ovarian syndrome. The ultrasounds were normal, and maternal serologies were negative. A dose of corticosteroids (intramuscular betamethasone) was given for pulmonary maturation 24 hours before birth. The delivery was eutocic, of cephalic presentation and 7 hours amniorrhexis. Apgar score was 7/9. Umbilical artery pH was 6.91. She required resuscitation with continuous positive pressure in the delivery room.

On the CBC, white blood cell count was 43,740/mm<sup>3</sup> (65% S, 3% NS, 1% Eo, 24% L, 7% Mo), and the C Reactive Protein (CRP) was 35.8 mg/L. It was carried out a microbiological study (hemoculture, peripheral smears) and empiric antibiotic treatment with ampicillin and gentamicin for 10 days. It was observed a progressive decrease in CRP from the 4<sup>th</sup> day of life. In contrast, there was a progressive elevation of leukocytes (maximum of 109,000 /mm<sup>3</sup> on the 5<sup>th</sup> day of life) (Table 1). A peripheral blood study didn't shown malignancy.

### Case 2

A 28-week gestational male newborn admitted to the neonatal intensive care unit for extreme prematurity and respiratory distress. It was the third gestation of a 28 years old woman. The gestation control was poor and she was amphetamine consumer.

**Table 1:** Evolution of the leukocyte formula and C-reactive protein (CRP) in both newborns.

	1dol <sup>a</sup>	2dol <sup>a</sup>	3dol <sup>a</sup>	4dol <sup>a</sup>	5dol <sup>a</sup>	6dol <sup>a</sup>	9dol <sup>a</sup>	13dol <sup>a</sup>
<b>Leukocytes (mm<sup>3</sup>)</b>								
Case 1	43.740	71.080		89.360	109.000			37.800
Case 2	26.030	64.620	72.170	86.000	97.340	72.570	27.550	
<b>Segmented (%)</b>								
Case 1	65%	58%		74%	88%			68%
Case 2	60%	49%	41%	71%	72%	74%	49%	
<b>Non segmented (%)</b>								
Case 1	3%	1%		3%	5%			2%
Case 2	0%	8%	3%	0%	0%	2%	0%	
<b>Lymphocytes (%)</b>								
Case 1	24%	23%		12%	4%			21%
Case 2	24%	27%	3%	27%	24%	19%	48%	
<b>Monocytes</b>								
Case 1	7%	18%		10%	3%			6%
Case 2	15%	13%	20%	2%	4%	5%	3%	
<b>Eosinophils (%)</b>								
Case 1	1%	0%		0%	0%			3%
Case 2	1	0%	0%	0%	0%	0%	0%	
<b>Basophiles (%)</b>								
Case 1	0%	0%		0%	0%			0%
Case 2	0%	0%	0%	0%	0%	0%	0%	
<b>CRP (mg/L)</b>								
Case 1	35,8	16,2		3	1,6			
Case 2	10,4	6,3	3,3	2	0,7	0,5		

<sup>a</sup>dol:days of life

Urine culture on the delivery day was positive for *E. Coli* sensitive to gentamicin. Corticosteroids were given for pulmonary maturation 24 hours before birth. The delivery was eutocic, of cephalic presentation, and 50 hours amniorrhexis. Apgar score was 7/9. Umbilical artery pH was 7.39. He was born vigorous but he stank. No resuscitation was required and continuous positive pressure was initiated.

Chorioamnionitis was suspected and peripheral smears and hemoculture were collected. Empiric antibiotic treatment with ampicillin and gentamicin was initiated. At the third day, due to alterations in the white blood cell count, the antibiotherapy was changed to ampicillin and cefotaxime for two more days. Positive cultures were obtained for *Mycoplasma hominis* and *Ureaplasma urealyticum* in the smears of the fetal and maternal faces of the placenta and the otic smear. The white blood cell count increased up to 7,340/mm<sup>3</sup> on the fifth day of life, without elevation of the CRP value (Table 1). A peripheral blood study didn't shown malignancy.

### Commentary

In both cases, it was suspicion of infection and antibiotic treatment was given early. A differential diagnosis with onco-hematologic pathology was

performed due the progressive increase in leukocytes >50,000/mm<sup>3</sup>, with no signs of malignancy in any of the cases.

In the case of a newborn with extreme hyperleukocytosis, if clinical history, physical examination and peripheral blood extension study are not indicative of leukemia, myeloproliferative disorder or a leukocyte adhesion defect, expectant management may be maintained [3,4].

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