



Sézary syndrome

GENERAL POINTS

- Among the primary cutaneous lymphomas, mycosis fungoides (MF) represents 44% of cases and Sézary syndrome (SS) 3% of cases. SS is often primary and rarely preceded by MF.
- Age at diagnosis > 60 years (predominantly in males).
- Overall survival at 5 years is 88% for MF and 24% for SS.

CLINICAL/BIOLOGICAL PRESENTATION

➔ Definition

- Diagnosis based on a series of arguments (skin, lymph, blood, organs).
- Sézary syndrome corresponds to a stage \geq IVA1 of the ISCL/EORTC classification proposed in 2007⁴⁰ and revised by the EORTC in 2018⁴¹.

Sézary syndrome:			
Cutaneous involvement (T1-4)	Associated with	B2	= stage IVA1
		B0/B1 + N3	= stage IVA2
		B0/B1 + M1	= stage IVB

➔ Clinical signs

- Cutaneous involvement (T1-4):
 - the most useful approach for management is to distinguish between patients with or without erythroderma (stages T1-3 and T4, respectively). Stages T1-3 correspond to the presence of macules/papules/plaques or skin tumours. Stage T4 corresponds to the presence of diffuse erythema \geq 80% of body surface area. The majority of SS correspond to stage T4;
 - approximately 50% of erythroderma patients are B2 (= SS) and 50% are B0/B1 (= MF). The distinction between B0/B1 vs. B2 has a major prognostic and therapeutic impact;



- the majority of non-erythroderma patients are B0/B1 (= MF). Fewer than 2% are B2 (= SS). There is no consensus on the prognostic impact of dissemination in the peripheral blood in this patient category.
- Nodal involvement (N0-3):
 - Peripheral lymphadenopathy is very common in SS;
 - the presence of peripheral lymphadenopathy with partial or total disappearance of nodal structure (stage N3) causes patients to be automatically classed as SS.
- Organ involvement (M0-1):
 - organ involvement is common in SS (liver, spleen, lung, etc.);
 - the presence of organ involvement (stage M1) automatically causes patients to be classed as SS.

➔ Complete blood count

- Presence of Sézary cells:
 - defined and quantified by morphology and/or phenotype;
 - stages defined by the ISCL/EORTC classifications (2007, 2018).

Stage	Morphology	Immunophenotype
B0	SC < $1 \times 10^9/L$ and $\leq 5\%$ ± T clonality	CD4+ CD7- OR CD4+ CD26- < $0.25 \times 10^9/L$ + proven T clonality
B1	SC < $1 \times 10^9/L$ and > 5% + proven T clonality OR SC $\geq 1 \times 10^9/L$ + absence of T clonality	CD4+ CD26- OR CD4+ CD26- between the 2 + proven T clonality
B2	SC $\geq 1 \times 10^9/L$ + proven T clonality	CD4+ CD26- OR CD4+ CD26- $\geq 1 \times 10^9/L$ + proven T clonality

- Remainder of CBC:
 - rare lymphocytosis and cytopenia;
 - eosinophilia in 20% of cases.

INTERPRETATION OF ADDITIONAL TESTS

<p>Morphology</p>	<ul style="list-style-type: none"> • Cells to be investigated in the thinly spread zones of the blood smear • Percentage of Sézary cells defined relative to the total lymphocyte count • Typically, the cells are small to medium in size and have a cerebriform nucleus, dense chromatin, lighter than a normal lymphocyte, presenting one or more grooves. Large-sized cells are observed in 32 to 67% of cases • Small quantities of Sézary cells may be observed in certain benign dermatoses (eczema, psoriasis) and levels $> 1 \times 10^9/L$ in certain benign erythrodermas
<p>Immunophenotyping</p>	<ul style="list-style-type: none"> • Proliferation of CD4+, CD45RO+ cells most frequently • T4/T8 ratio > 10 in 80% of cases • CD4+ CD7- clone $> 40\%$ in half of cases • CD4+ CD26- clone $> 30\%$ (PPV and Sp $\approx 100\%$) • CD4+ CD26- CD27+ clone highly evocative • CD3+ CD158k+ clone highly sensitive and very specific • The majority of the abnormalities described may be observed in benign erythroderma; notably a T4/T8 ratio > 10, a CD4+ CD7- clone $< 40\%$ or a CD4+ CD26- clone $< 30\%$
<p>Genetics</p>	<ul style="list-style-type: none"> • Clonal rearrangement of TCR (Se $> 75\%$, Sp $> 90\%$). A blood T clone identical to that found in skin is a strong argument. An isolated T clone or different to the skin clone has little diagnostic value • Frequent complex karyotype in advanced forms