

Supplementary Material 1. Methodology of literature review and data analysis.

Literature search

Aim of this literature review was to compile reported information regarding adult-onset AML, i.e. published reports of adult patients with isolated cutaneous myeloid sarcoma (icMS) or aleukemic leukemia cutis (ALC) as the earliest manifestation of an acute myeloid leukemia (AML) in order to highlight the disease characteristics of these rare conditions and contribute to their clinical recognizability. Only cases were considered in which at the time of the confirmation of the cutaneous leukemia infiltration an AML could not be diagnosed in either blood or bone-marrow studies. A search of the databases PubMed and Scopus from January 1985 to December 2022 was conducted to identify English-language publications reporting adult patients (older than 18 years) with ‘specific’ skin involvement in the course of AML employing separately the search merges primary OR isolated myeloid sarcoma skin OR primary OR isolated granulocytic sarcoma skin OR primary OR isolated chloroma skin OR aleukemic leukemia cutis. In line with the definition of the ‘aleukemic’ skin involvement, the initial output of N=251 publications were subsequently searched after exclusion of the duplicates (N=37) in a two-step procedure, initially by title/abstract (N=111) and subsequently by text content for reports of cases of cutaneous MS/ALC preceding adult-onset AML (N=103), i.e. cases in which the AML could first be diagnosed in the peripheral blood and/or the bone marrow distinctly after the confirmation of the skin involvement. Only reports with adequate description of the clinical data were included; studies which just mentioned icMS or ALC without detailed clinical information were not considered in this review. Literature retrieval and data extraction were conducted by two authors independently (K. M. and S. G.) and data were compiled using descriptive statistics. A total of 14 publications were

identified that reported 15 cases fulfilling the inclusion criteria of this study.

Statistical analysis

Descriptive statistics, Mann-Whitney U test, runs test [cutoff: median] for time series, Kaplan-Meier times-to-events evaluations with Log Rank (Mantel-Cox) test and Cox proportional hazard models were calculated with the statistical package SPSS (IBM, Chicago IL, USA) and were interpreted at probability level $p < 0.05$.