

# Leukaemia Section

## Review

## Myeloid sarcoma

Karen M. Chisholm

Department of Laboratories, Seattle Childrens Hospital, Seattle, WA, USA;  
karen.chisholm@seattlechildrens.org

Published in Atlas Database: September 2018

Online updated version : <http://AtlasGeneticsOncology.org/Anomalies/MyeloidSarcomaID1822.html>

Printable original version : <http://documents.irevues.inist.fr/bitstream/handle/2042/70458/09-2018-MyeloidSarcomaID1822.pdf>

DOI: 10.4267/2042/70458

This work is licensed under a Creative Commons Attribution-Noncommercial-No Derivative Works 2.0 France Licence.  
© 2019 Atlas of Genetics and Cytogenetics in Oncology and Haematology

### Abstract

Review on myeloid sarcoma, with data on clinics, pathology, and involved genes.

#### Keywords

chloroma, extramedullary myeloid tumor, granulocytic sarcoma, myeloid sarcoma

### Identity

Myeloid sarcoma

#### Other names

Granulocytic sarcoma

Chloroma

Extramedullary myeloid tumor

### Clinics and pathology

#### Disease

Myeloid sarcoma is defined as a proliferation of myeloblasts effacing tissue architecture and forming a mass in a site other than bone marrow. Originally termed "chloroma" due to the greenish hue appreciated grossly owing to the production of myeloperoxidase, it has also been called granulocytic sarcoma (due to immature to maturing granulocytes, usually consistent with an acute myeloid leukemia with maturation, French-American-British subtype M2), and extramedullary myeloid tumor. In skin, this entity has been referred to as leukemia cutis. However, the most recent and most encompassing term is myeloid sarcoma; while this entity can consist of myeloblasts (with or without maturation), it can also consist of monoblasts or myelomonocytes, and rarely erythroid precursors or megakaryoblasts.

#### Phenotype/cell stem origin

The cells of origin are hematopoietic stem cells/progenitor cells.

#### Etiology

The etiology of myeloid sarcoma is similar to that of acute myeloid leukemia, but instead is present in an extramedullary site.

#### Epidemiology

Myeloid sarcoma can occur at any age, but does appear more frequent in children and in older patients. Some reports give a slightly increased male predominance (Pileri et al., 2007; Kawamoto et al., 2016). Myeloid sarcoma is thought to occur in 1.4-9% of patients with AML (Alexiev et al., 2007). In children, the rate of isolated myeloid sarcoma is approximately 1.3%, while the rate of isolated myeloid sarcoma preceding AML is approximately 2.5% (Reinhardt and Creutzig, 2002). Myeloid sarcoma occurs in 6.7%-23.3% of children with a concurrent diagnosis of AML (Dusenbery et al., 2003; Johnston et al., 2012; Stve et al., 2017).

#### Clinics

Myeloid sarcoma is thought to occur in four different scenarios: 1) de novo in the absence of any underlying acute myeloid leukemia or other myeloid neoplasm; 2) concurrently with acute myeloid leukemia (sometimes the first sign of disease); 3) representing blast crisis or blast transformation in myeloproliferative disorders or myelodysplastic syndromes; 4) representing relapse AML (often post-transplant). The latter scenario occurs in 5-12% of patients after allogeneic stem cell transplantation, accounting for 7-46% of post-transplant AML relapses (Solh et al., 2016). Approximately 27% of

patients present with de novo/isolated disease (Pileri et al., 2007). Some reports have identified myeloid sarcoma in patient with concurrent non-Hodgkin's lymphoma or with a history of a non-hematopoietic tumor (Pileri et al., 2007).

Myeloid sarcoma can occur anywhere in the body (except for the bone marrow), but has been found to be most frequent in the skin, lymph nodes, bone, soft tissue, gastrointestinal tract, and mediastinum, with less frequent sites including the testes (Traweek et al., 1993; Pileri et al., 2007; Kawamoto et al., 2016). Multiple sites of involvement may occur in the same individual at the same time. In children, the orbit is an additional common site (Reinhardt and Creutzig, 2002; Dusenbery et al., 2003; Johnston et al., 2012; Støve et al., 2017).

Symptoms of myeloid sarcoma depend on the site of involvement.

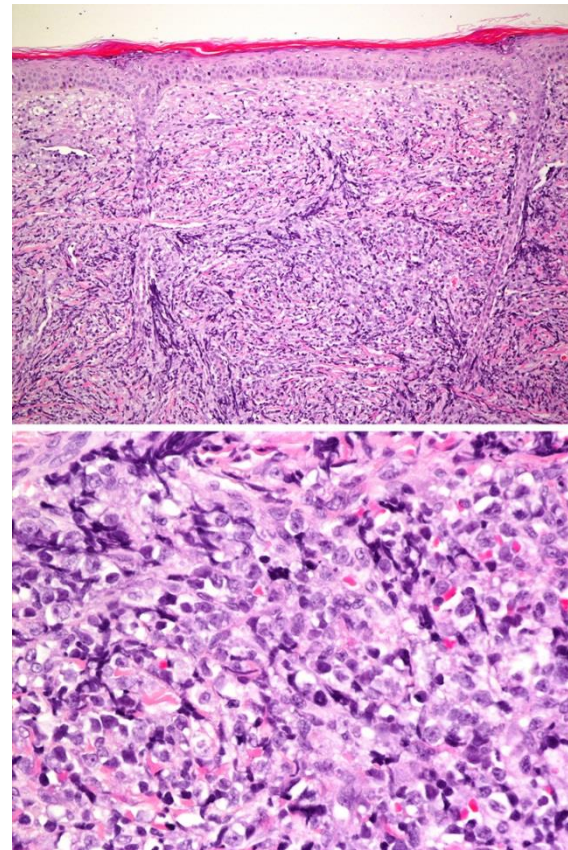
### Cytology

As stated previously, the cells can be myeloblasts, differentiating granulocytes (ex. promyelocytes), a mixture of myeloblasts and monoblasts, pure monoblasts, or cells with monocytic differentiation. Rarely myeloid sarcomas consist of erythroblasts or megakaryoblasts. The cells are usually medium to large in size with high nuclear-to-cytoplasmic ratios, fine to vesicular chromatin, variably prominent nucleoli, and scant cytoplasm which may contain granules. Nuclei with irregular or indented contours may represent monocytic cells.

### Pathology

By definition, myeloid sarcoma consists of blasts forming a mass in extramedullary tissue. Depending on the tissue, the cells may be present in confluent sheets, nests, or in cords divided by fibrous septae. In lymph nodes, they can efface the architecture or be present infiltrating the paracortex and sinuses. In the spleen, the neoplasm usually infiltrates the red pulp with persistent white pulp. In some cases, eosinophilic myelocytes and a variety of granulocyte precursors can be seen intermixed with the blasts. The blasts may accumulate around blood vessels and may even invade blood vessel walls. Mitoses may be readily identifiable and tingible body macrophages may be present. Of note, in those cases with isolated myeloid sarcoma, bone marrow blasts may be present at

By morphology, the sarcoma can usually be classified as acute myeloid leukemia with maturation, acute myelomonocytic leukemia, or acute monoblastic/monocytic leukemia. The myeloid sarcomas of the skin are often myelomonocytic or monoblastic/monocytic (Reinhardt and Creutzig, 2002; Pileri et al., 2007). Those in the orbit in pediatrics are often acute myeloid leukemia with maturation.



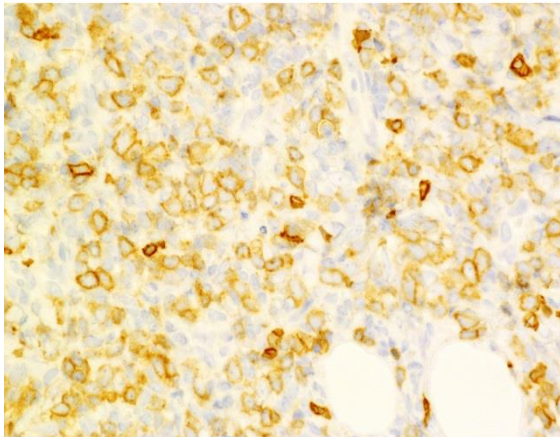
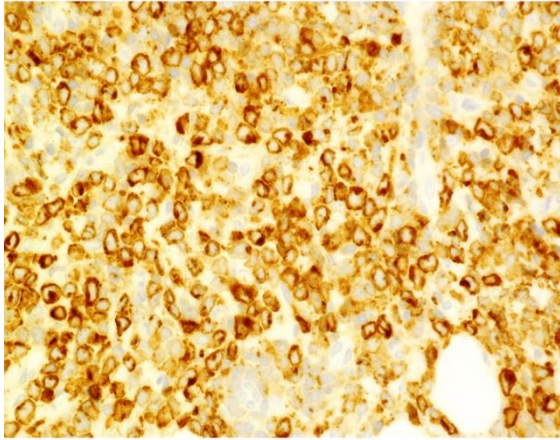
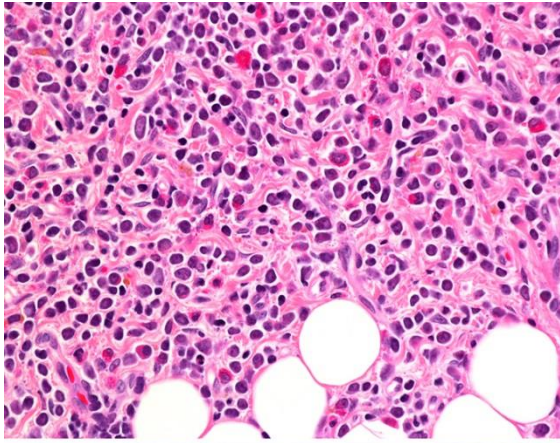
**Figure 1:** Leukemia cutis, or myeloid sarcoma of the skin. Left panel is low power magnification and right panel is high power magnification demonstrating an infiltrate of atypical cells with round to irregular nuclear contours, fine chromatin, conspicuous nucleoli, and pale cytoplasm.

### Treatment

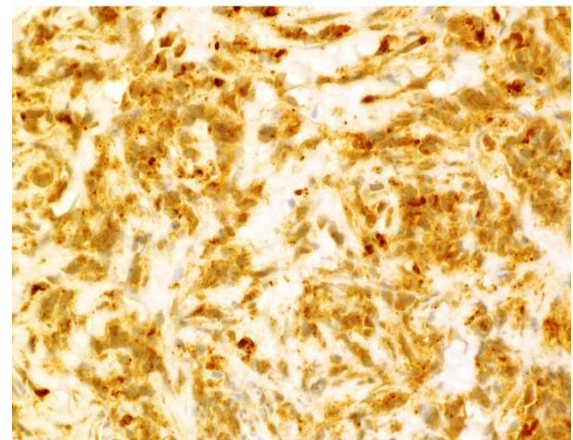
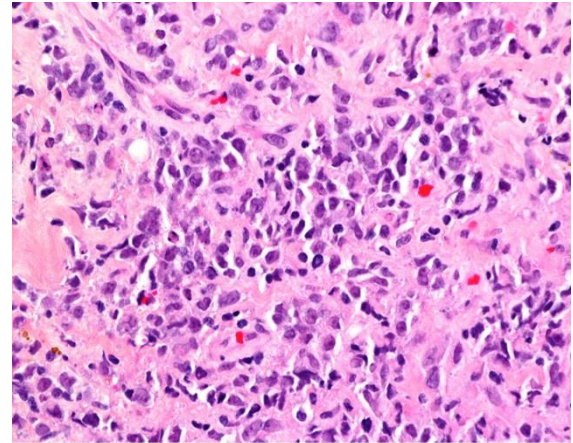
The treatment for myeloid sarcoma is the same as that for acute myeloid leukemia, which includes induction systemic chemotherapy (Bakst et al., 2011). Cytogenetic and molecular data are important for risk stratification, similar to AML. For those with intermediate or high risk disease, allogeneic transplant may be considered (Solh et al., 2016).

Local radiation has not been found to be beneficial in induction therapy, but has been useful in consolidation if a complete response has not been achieved with chemotherapy. Radiation may also be of use in situations where debulking or rapid symptom relief from compression are needed prior to induction chemotherapy, or when there is recurrence after transplant. Surgery could also be performed if rapid debulking is required. (Bakst et al., 2011)





**Figure 2:** Soft tissue mass demonstrating a proliferation of immature myeloid cells into adipose tissue. Scattered eosinophilic myelocytes are also present in this myeloid sarcoma with t(8;21). The middle panel demonstrates immunohistochemical staining for myeloperoxidase which is positive. The right panel demonstrates positivity for CD117 immunohistochemical staining.



**Figure 3:** Biopsy of soft tissue near the left knee demonstrates an infiltrate of medium sized cells with irregular nuclear contours, open chromatin, variably prominent nucleoli, and eosinophilic cytoplasm. Immunohistochemical staining for lysozyme is positive (second panel). This myeloid sarcoma represented an extramedullary relapse after transplantation in a patient with AML with KMT2A gene rearrangement (MLL on chromosome 11q23).

**Treatment**

The treatment for myeloid sarcoma is the same as that for acute myeloid leukemia, which includes induction systemic chemotherapy (Bakst et al., 2011). Cytogenetic and molecular data are important for risk stratification, similar to AML. For those with intermediate or high risk disease, allogeneic transplant may be considered (Solh et al., 2016). Local radiation has not been found to be beneficial in induction therapy, but has been useful in consolidation if a complete response has not been achieved with chemotherapy. Radiation may also be of use in situations where debulking or rapid symptom relief from compression are needed prior to induction chemotherapy, or when there is recurrence after transplant. Surgery could also be performed if rapid debulking is required. (Bakst et al., 2011)

## Evolution

If isolate myeloid sarcoma is not treated, it will usually evolve into acute myeloid leukemia within 5 to 12 months.

## Prognosis

In patients with concurrent AML, the additional clinical finding of myeloid sarcoma has not been found to have clinical significance (Traweek et al., 1993; Kawamoto et al., 2016). A possible exception is in adult patients with the t(8;21) translocation in which myeloid sarcoma associated with leukemia has a worse prognosis than the leukemia alone (Byrd et al., 1997). However, in children, isolated myeloid sarcoma has been found to have better prognosis than similarly aged children with acute myeloid leukemia (Dusenbery et al., 2003). Additionally, children with orbital myeloid sarcoma have a higher overall survival compared to myeloid sarcoma from other sites, even after adjustment for cytogenetics (Johnston et al., 2012).

In adults, studies have varied, with some demonstrated increased survival, others worse survival, and others no change in outcomes of isolated myeloid sarcoma cases compared to acute myeloid leukemia not associated with myeloid sarcoma (Wilson and Medeiros, 2015); however, two studies did show increased overall survival for those with isolated myeloid sarcoma (Tsimberidou et al., 2008; Movassaghian et al., 2015). Kawamoto et al. (2016) found that those with myeloid sarcoma representing blast crisis or blast transformation in myeloproliferative disorders or myelodysplastic syndromes have a worse prognosis than myeloid sarcoma with or without concurrent AML.

## Cytogenetics

### Cytogenetics morphological

Studies have shown that approximately 55% of cases have karyotypic abnormalities (Pileri et al., 2007). Similar to acute myeloid leukemia, myeloid sarcoma can have recurrent genetic abnormalities, including t(8;21)(q22;q22.1) (RUNX1 / RUNX1T1), inv(16)(p13.1q22) (CBFB / MYH11), and KMT2A (11q23) gene rearrangements. Other karyotypic abnormalities include monosomy 7 and trisomy 8. Those with t(8;21) are more often located in the orbit and associated with pediatric cases; these cases represent acute myeloid leukemia with maturation (Reinhardt and Creutzig, 2002). Cases with inv(16) tend to involve the intestine, breast, or uterus and are also associated with foci of plasmacytoid dendritic cells (Pileri et al., 2007). Cases with KMT2A translocations more often involve the skin or breast, and are usually myelomonocytic or monoblastic/monocytic in morphology. Those with t(9;22)(q34.1;q11.2) (BCR / ABL1) are associated

with chronic myelogenous leukemia in blast phase, and most commonly occur in lymph nodes (Wilson and Medeiros, 2015).

## References

- Alexiev BA, Wang W, Ning Y, Chumsri S, Gojo I, Rodgers WH, Stass SA, Zhao XF. Myeloid sarcomas: a histologic, immunohistochemical, and cytogenetic study *Diagn Pathol* 2007 Oct 31;2:42
- Audouin J, Comperat E, Le Tourneau A, Camilleri-Brot S, Adida C, Molina T, Diebold J. Myeloid sarcoma: clinical and morphologic criteria useful for diagnosis *Int J Surg Pathol* 2003 Oct;11(4):271-82
- Bakst RL, Tallman MS, Douer D, Yahalom J. How I treat extramedullary acute myeloid leukemia *Blood* 2011 Oct 6;118(14):3785-93
- Byrd JC, Weiss RB, Arthur DC, Lawrence D, Baer MR, Davey F, Trikha ES, Carroll AJ, Tantravahi R, Qumsiyeh M, Patil SR, Moore JO, Mayer RJ, Schiffer CA, Bloomfield CD. Extramedullary leukemia adversely affects hematologic complete remission rate and overall survival in patients with t(8;21)(q22;q22): results from Cancer and Leukemia Group B 8461 *J Clin Oncol* 1997 Feb;15(2):466-75
- Dusenbery KE, Howells WB, Arthur DC, Alonzo T, Lee JW, Kobrinsky N, Barnard DR, Wells RJ, Buckley JD, Lange BJ, Woods WG. Extramedullary leukemia in children with newly diagnosed acute myeloid leukemia: a report from the Children's Cancer Group *J Pediatr Hematol Oncol* 2003 Oct;25(10):760-8
- Falini B, Lenze D, Hasserjian R, Coupland S, Jaehne D, Soupir C, Liso A, Martelli MP, Bolli N, Bacci F, Pettrossi V, Santucci A, Martelli MF, Pileri S, Stein H. Cytoplasmic mutated nucleophosmin (NPM) defines the molecular status of a significant fraction of myeloid sarcomas *Leukemia* 2007 Jul;21(7):1566-70
- Johnston DL, Alonzo TA, Gerbing RB, Lange BJ, Woods WG. Superior outcome of pediatric acute myeloid leukemia patients with orbital and CNS myeloid sarcoma: a report from the Children's Oncology Group *Pediatr Blood Cancer* 2012 Apr;58(4):519-24
- Kawamoto K, Miyoshi H, Yoshida N, Takizawa J, Sone H, Ohshima K. Clinicopathological, Cytogenetic, and Prognostic Analysis of 131 Myeloid Sarcoma Patients *Am J Surg Pathol* 2016 Nov;40(11):1473-1483
- Movassaghian M, Brunner AM, Blonquist TM, Sadrzadeh H, Bhatia A, Perry AM, Attar EC, Amrein PC, Ballen KK, Neuberg DS, Fathi AT. Presentation and outcomes among patients with isolated myeloid sarcoma: a Surveillance, Epidemiology, and End Results database analysis *Leuk Lymphoma* 2015 Jun;56(6):1698-703
- Pileri SA, Ascani S, Cox MC, Campidelli C, Bacci F, Piccioli M, Piccaluga PP, Agostinelli C, Asioli S, Novero D, Bisceglia M, Ponzoni M, Gentile A, Rinaldi P, Franco V, Vincelli D, Pileri A Jr, Gasbarra R, Falini B, Zinzani PL, Baccarani M. Myeloid sarcoma: clinico-pathologic, phenotypic and cytogenetic analysis of 92 adult patients *Leukemia* 2007 Feb;21(2):340-50
- Reinhardt D, Creutzig U. Isolated myelosarcoma in children-update and review *Leuk Lymphoma* 2002 Mar;43(3):565-74
- Seifert RP, Bulkeley W 3rd, Zhang L, Menes M, Bui MM. A practical approach to diagnose soft tissue myeloid sarcoma

preceding or coinciding with acute myeloid leukemia *Ann Diagn Pathol* 2014 Aug;18(4):253-60

Solh M, Solomon S, Morris L, Holland K, Bashey A. Extramedullary acute myelogenous leukemia *Blood Rev* 2016 Sep;30(5):333-9

Stve HK, Sandahl JD, Abrahamsson J, Asdahl PH, Forestier E, Ha SY, Jahnukainen K, Jnsson G, Lausen B, Palle J, Zeller B, Hasle H. Extramedullary leukemia in children with acute myeloid leukemia: A population-based cohort study from the Nordic Society of Pediatric Hematology and Oncology (NOPHO) *Pediatr Blood Cancer* 2017 Dec;64(12)

Traweek ST, Arber DA, Rappaport H, Brynes RK.

Extramedullary myeloid cell tumors An immunohistochemical and morphologic study of 28 cases *Am J Surg Pathol*

Tsimberidou AM, Kantarjian HM, Wen S, Keating MJ, O'Brien S, Brandt M, Pierce S, Freireich EJ, Medeiros LJ, Estey E. Myeloid sarcoma is associated with superior event-free survival and overall survival compared with acute myeloid leukemia *Cancer* 2008 Sep 15;113(6):1370-8

Wilson CS, Medeiros LJ. Extramedullary Manifestations of Myeloid Neoplasms *Am J Clin Pathol* 2015 Aug;144(2):219-39

---

*This article should be referenced as such:*

Chisholm KM. Myeloid Sarcoma. *Atlas Genet Cytogenet Oncol Haematol*. 2019; 23(6):149-153.

---