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LETTER TO THE EDITOR

Juvenile myelomonocytic leukemia: a surprising cause of peri-orbital tumor and squint

Anselm Chi-wai Lee[1] · Seo Wei Leo[2]

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Dear Editor,

Juvenile myelomonocytic leukemia (JMML) is a rare hemic malignancy in children. It typically presents with fever, skin lesions, hepatosplenomegaly, and hyperleukocytosis with signs of marrow failure [1]. Distracting extramedullary disease may potentially delay diagnosis. Ocular involvement has been rarely reported in JMML, either at disease progression after diagnosis [2] or at relapse after stem cell transplantation [3]. Our patient is unique as she presented primarily with ocular manifestations while hematologic changes were subtle.

A 19-month-old girl with no stigmata of neurofibromatosis presented with bilateral proptosis, left abducens nerve palsy, and prolonged fever for 2 weeks. There was no external swelling. No significant lymphadenopathy or hepatosplenomegaly was found and there were no other neurologic deficits. Computed tomography showed soft tissue swelling infiltrating the orbits on both sides with intra-orbital and intracranial, extradural masses (Fig. 1a). She was evacuated to our hospital from Cambodia for further management with an initial suspicion of metastatic neuroblastoma. Her complete blood count revealed hemoglobin 9.9 g/dL, WBC 22.81×10^9/L, and platelet 192×10^9/L. The peripheral blood smear showed a leucoerythroblastic picture with blasts 1%, promyelocytes 30%, myelocytes 6%, monocytes 14%, neutrophils 32%, and lymphocytes 17% (Fig. 1b). The bone marrow was marked by myeloid hyperplasia with predominantly promyelocytes (60%) but no excess of blasts (< 1%). Atypical monocytes constituted 14% of the nucleated cells. On flow cytometry, 13% of the promyelocytes had an aberrant expression of cyCD3, while monocytes were HLA-DR-negative. RT-PCR for transcripts of BCR-ABL and PML-RARα was negative, but an aberrant karyotype with 46XX,inv(3)(p25q27),t(7;12)(q32;q22) was found in 17 out of 20 metaphases analyzed. The translocation and a similar inversion, inv(3)(p24q26), have been reported previously in myeloid malignancies. The cerebrospinal fluid was acellular and negative for malignancy. Fetal hemoglobin was normal for age (2.6%). She was therefore diagnosed as juvenile myelomonocytic leukemia. While awaiting for transplantation, the total WBC was maintained below 30×10^9/L with daily 6-mercaptopurine 50mg/m^2/day orally, and two cycles of cytarabine 3 g/m^2 12-hourly for 3 days 2 months apart. At 5 months after diagnosis, she received a matched unrelated donor cord blood transplantation after conditioning with busulfan, fludarabine, melphalan, and rabbit antithymocyte globulin. Graft-versus-host disease prophylaxis was with cyclosporine alone. She engrafted successfully with complete donor chimerism and remained in first complete remission afterwards. The peri-orbital tumor was gradually resolved during first 6 months post-transplant without additional treatment, but the left paralytic esotropia was not reversible and required surgical correction. The eye alignment remained good 4 years post strabismus surgery.

Extramedullary disease other than cutaneous and hepatosplenic infiltration at diagnosis in JMML is uncommon. Tumor-like presentation has been reported as bilateral breast masses [4], colonic nodules with intractable diarrhea [5], or massive cervical lymphadenopathy [6]. Pulmonary infiltration with respiratory distress may be confused with chest infections [7]. JMML involving the eye or the central nervous system is rare. Choroidal infiltration in JMML was first described in a 12-month-old boy with the leukemia progressing

✉ Anselm Chi-wai Lee
anselm.cw.lee@gmail.com

[1] Children's Haematology and Cancer Centre, Mount Elizabeth Hospital, Level 4, 3 Mount Elizabeth, Singapore 228510, Singapore

[2] Dr Leo Adult & Paediatric Eye Specialist Pte Ltd, Mount Elizabeth Medical Centre, Singapore, Singapore

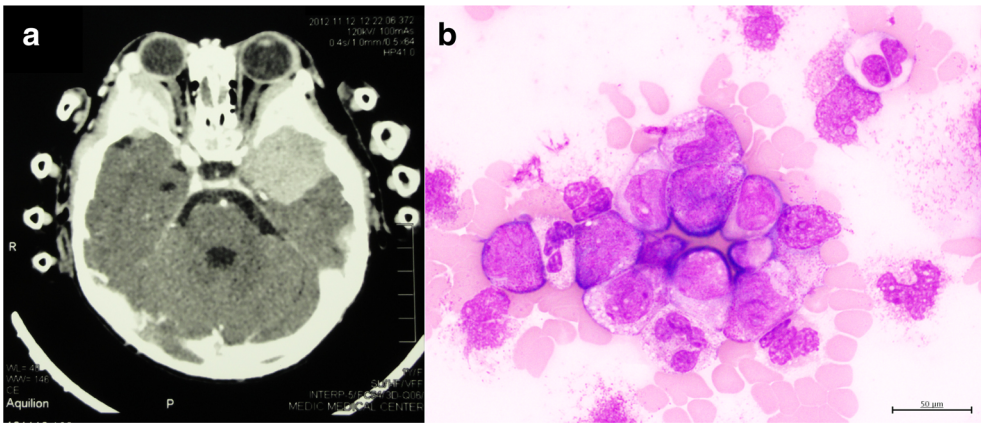

Fig. 1 **a** CT head showing contrast-enhanced soft tissue masses infiltrating the lateral walls of both orbits, with intra-orbital masses abutting the globes, and intracranial, extradural extensions that is more prominent on the left side. **b** Photomicrograph (Wright's, × 100) of the peripheral blood smear showing predominantly promyelocytes and atypical monocytes

after 11 months of diagnosis [2]. He survived the leukemia after bone marrow transplantation but was nevertheless left blind. Retinal infiltration was reported in another 3-year-old boy 2 years into diagnosis, with relapse documented after stem cell transplantation [3]. He succumbed to the disease 4 months later. The peri-orbital masses and abducens nerve palsy in this case is unique and may potentially be confused with metastatic neuroblastoma, Langerhans cell histiocytosis, or soft tissue sarcomas.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Study involving animals or human subjects Not applicable.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors. As such, in our institution, approval by the institutional review board is not needed. On similar terms, informed consent other than medical management is not required.

References

1. Sakashita A, Matsuda K, Koike K (2016) Diagnosis and treatment of juvenile myelomonocytic leukemia. Pediatr Int 58(8):681–690
2. Nambu M, Shimizu K, Ito S, Ohta S (1999) A case of juvenile myelomonocytic leukemia with ocular infiltration. Ann Hematol 78(12):568–570
3. Chang GC, Moshfeghi DM, Alcorn DM (2006) Choroidal infiltration in juvenile myelomonocytic leukemia. Br J Ophthalmol 90(8): 1067
4. Edison MN, O'Dell MC, Letter HP, Scherer K, Williams JL (2017) Juvenile myelomonocytic leukemia presenting as bilateral breast masses. Pediatr Radiol 47(1):104–107
5. Urs L, Stevens L, Kahwash SB (2008) Leukemia presenting as solid tumors: report of four pediatric cases and review of the literature. Pediatr Dev Pathol 11(5):370–376
6. Imamura T, Matsuo S, Yoshihara T, Chiyonobu T, Mori K, Ishida H, Nishimura Y, Kasubuchi Y, Naya M, Morimoto A, Hibi S, Imashuku S (2004) Granulocytic sarcoma presenting with severe adenopathy (cervical lymph nodes, tonsils, and adenoids) in a child with juvenile myelomonocytic leukemia and successful treatment with allogeneic bone marrow transplantation. Int J Hematol 80(2):186–189
7. Gustafsson B, Hellebostad M, Ifversen M, Sander B, Hasle H (2011) Acute respiratory failure in 3 children with juvenile myelomonocytic leukemia. J Pediatr Hematol Oncol 33(8):e363–e367