Leukemia Research Reports 4 (2015) 42–44

Contents lists available at ScienceDirect

Leukemia Research Reports

journal homepage: www.elsevier.com/locate/lrr

Case report

Pseudo-Guillain–Barré syndrome masking acute myeloid leukemia relapse: Brief report and review

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ARTICLE INFO

Article history:
Received 25 April 2015
Received in revised form
17 May 2015
Accepted 27 May 2015
Available online 17 July 2015

Keywords:
Acute myeloid leukemia
Isolated central nervous system recurrence
Cerebrospinal fluid

ABSTRACT

Central nervous system (CNS) relapse is not a rare presentation in acute myeloid leukemia (AML) as its incidence ranges between 2% and 9%. It manifests with meningeal leukemia, cranial nerve palsies or cerebral mesenchymal myeloid sarcoma. We herein report the case of a 69 year-old female that presented a pseudo-Guillain–Barré syndrome masking an AML CNS relapse. Her symptoms completely resolved upon administration of a tailored treatment. This case suggests that puzzling neurological manifestations in patients with a history of AML should be considered as a CNS recurrence and investigated accordingly even in the context of normal imaging findings.

1. Introduction

Acute myeloid leukemias (AML), stratified into different risk categories based on cytogenetic and biomolecular analysis, respond differently to therapeutic interventions implemented for curative intent. Overall, most AML patients have complete remission but 40% commonly relapse during the first three years [1]. It occurs most often in the bone marrow (BM) but central nervous system (CNS) involvement is not rare as its incidence ranges between 2% and 9% [2]. CNS leukemia can present as meningeal leukemia, cranial nerve palsies or cerebral mesenchymal myeloid sarcoma [3]. Peripheral neuropathy may also be a puzzling manifestation as it is a common complaint in clinical practice with a very wide differential diagnosis.

2. Case presentation

We report the case of an otherwise healthy 69 year-old female patient that presented to our department for a new onset of persistent disabling fatigue and 10% weight loss over two months. She had no prior medical problems and did not complain of any other symptoms. On clinical exam, the patient was afebrile, hypotensive with a blood pressure of 90/50 mmHg, and tachycardic at 140 beats/min. Her initial labs showed hemoglobin 3 g/dL, white blood cells 114.000×10^9/L with 80% blasts, platelets of 15.000×10^9/L, LDH of 773 U/L, SGOT of 1400 U/L and SGPT of 1416 U/L. She had increased PT and PPT with low fibrinogen level suggestive of disseminated intravascular coagulation. Qualitative RT-PCR on BM cytology revealed the presence of *CBFβ-MYH11* transcript type D (chromosome 16 inversion), and *FLT3*p.D835V mutation confirming an acute myelomonocytic leukemia (AML/M4). BM cytogenetic analysis using R banding revealed a translocation between chromosomes 5 and 12, 46,XX,t(5;12)(p13;p13). Accordingly, the patient underwent 3+7 induction chemotherapy with cytarabine (100 mg/m^2 continuous infusion days 1–7) and idarubicin (9 mg/m^2 days 1–3) although she only received a single dose of the latter because of her abnormal liver function tests. Analysis of her BM one month later showed complete cytologic remission with persistence of *CBFβ-MYH11* fusion transcript. The patient received thereafter three consolidation cycles with high-dose cytarabine. Complete molecular response was obtained three months later.

One year after her initial diagnosis, the patient presented back for the abrupt onset of symmetrical bilateral lower-limb weakness and numbness. The patient did not report other symptoms or history of trauma. Clinical examination revealed a healthy person except for a symmetrical proximal and distal bilateral lower limbs weakness and sensory loss with absence of deep tendon reflexes. Complete blood count, LDH, and electrolytes were within normal range. Contrast enhanced magnetic resonance imagery (MRI) of her lumbar spine showed mild anterolisthesis of L4 on L5. Brain MRI was normal for her age. Nerve conduction studies

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http://dx.doi.org/10.1016/j.lrr.2015.05.002

demonstrated acute inflammatory demyelinating neuropathy suggestive of Guillain–Barré syndrome. Subsequently, we performed a lumbar puncture that revealed pleiocytosis with 405 blast cells according to cytology and flow cytometry. Analysis of her BM aspirate showed 3% of blasts with positive *CBFβ-MYH11* fusion transcript D, and reciprocal translocation between chromosomes 3 and 16 detected in 4% of examined cells,46,XX,t(3;16)(p14;q24)[2]/46,XX[48]. We retained the diagnosis of isolated AML CNS meningeal recurrence. Consequently, the patient received a chemotherapy protocol of standard FLAG-IDA dosage with intrathecal chemotherapy of methotrexate (10 mg) plus dexamethasone (5 mg) alternating with cytarabine (50 mg) twice weekly. The patient noted complete resolution of her symptoms and her clinical exam was back to normal three weeks after initiating chemotherapy. She remains alive after six months without any complains.

3. Discussion

Myelomonocytic and monocytic leukemias are the most common leukemia subtypes to affect extramedullary organs with CNS involvement occurring in 20% [4]. Leukemia cells affect the CNS by various mechanisms that may advocate specific treatment approaches. Blasts may infiltrate leptomeninges causing meningeal leukemia, cranial nerves inducing cranial nerve palsies, or may precipitate into a solid collection known as myeloid sarcoma [3]. Most commonly, patients with CNS leukemia are asymptomatic. Nevertheless, a small number of patients describe increased intracranial pressure manifesting with headache, stiff neck, mental derangement, papilloedema, nausea and vomiting. Case reports describe rare presentations of cranial nerve palsies and cauda equine syndrome [5–7].

Literature describes multiple risk factors for the occurrence of CNS relapse in adult patients with AML: French–American–British classification (FAB) M4/M5 subtypes, cytogenetic abnormality inversion 16, male sex, high white blood cell count at diagnosis, elevated serum lyzozyme and lactate dehydrogenase concentrations [2,8,9]. Aside from her gender, our patient had the other four mentioned risk factors. One recent paper reported a high prevalence of FLT3 mutations in AML patients with CNS relapse. Of particular significance is a recent multivariate analysis that demonstrated that the use of old instead of new generation therapeutic induction regimens is the only factor affecting CNS relapse [11].

In the absence of a consensus for the optimal therapy for adult AML CNS recurrence, treatment approaches are extrapolated from studies of paediatric AML and acute lymphoblastic leukemia (ALL). Generally, isolated CNS leukemia relapse is considered a systemic disease independently of the BM status and requires systemic chemotherapy as local control is not sufficient. The optimal regimen is guided by the clinical presentation and pathophysiology of the CNS AML relapse. One study subdivided patients into meningeal leukemia, cranial nerve palsy, and cerebral parenchymal myeloid sarcoma and tailored their treatments accordingly [3]. The study resulted in 70.6% CNS remission without affecting long-term survival (overall survival 6.64 months).

Aside from case reports, only three small series report this entity. The first paper by Holmes et al. in 1987 describing CNS relapse in acute myelomonocytic leukemia reports 35% CNS relapse at a median of 19 months after complete remission [9]. Another study showed CNS leukemia recurrence on follow up in 2.2% of cases, remitters had a median survival of 10 months whilst nonremitters survived two months only [10]. One last article by Cuadron et al. in 2011 examined 458 adult patients with a diagnosis of non-promyelocytic AML and reported CNS involvement at first relapse in six patients of whom only two cases had isolated CNS relapse. The overall 5-year cumulative incidence of CNS relapse is 1.3% with a median of seven months (range 1–16 months) [11].

4. Conclusion

To our knowledge, this is the first case that presents a pseudo-Guillain–Barré syndrome uncovering a CNS leukemia recurrence. As shown by our literature review, it deserves to be highlighted because it underlines the possibility of a rare and atypical presentation of AML recurrence. Moreover, our case suggests that puzzling neurological manifestations in patients with a history of AML should be investigated for CNS AML recurrence and not simply attributed to the neurotoxicity of chemotherapy. As in ALL, this eventuality should be considered in AML and prompt thorough investigations even in the context of normal imaging findings.

Authors' contribution

- Elie El Rassy: Review of literature and drafting.
- Fadi El Karak: Concept and treatment.
- Samer Tabchi: Review of literature and drafting.
- Eliane Chouery: Diagnosis and analysis of data.
- Andre Megarbane: Diagnosis and analysis of data.
- Joseph Kattan: Corrections and final approval.

Competing interests

The authors declare that they have no potential conflict of interest relevant to this article.

Acknowledgments

None.

References

[1] D. Verma, H. Kantarjian, S. Faderl, S. O'Brien, S. Pierce, K. Vu, et al., Late relapses in acute myeloid leukemia: analysis of characteristics and outcome, Leuk. Lymphoma 51 (5) (2010) 778–782.
[2] D.L. Johnston, T.A. Alonzo, R.B. Gerbing, B.J. Lange, W.G. Woods, Risk factors and therapy for isolated central nervous system relapse of pediatric acute myeloid leukemia, J. Clin. Oncol. Off. J. Am. Soc. Clin. Oncol. 23 (36) (2005) 9172–9178.
[3] C. Zheng, X. Liu, W. Zhu, X. Cai, J. Wu, Z. Sun, Tailored central nervous system-directed treatment strategy for isolated CNS recurrence of adult acute myeloid leukemia, Hematology 19 (4) (2014) 208–212.
[4] G. Specchia, F. Lo Coco, M. Vignetti, G. Avvisati, P. Fazi, F. Albano, et al., Extramedullary involvement at relapse in acute promyelocytic leukemia patients treated or not with all-trans retinoic acid: a report by the Gruppo Italiano Malattie Ematologiche dell'Adulto, J. Clin. Oncol. Off. J. Am. Soc. Clin. Oncol. 19 (20) (2001) 4023–4028.
[5] C. Fozza, F. Dore, M.A. Isoni, F. Longu, L. Dessì, L. Coppola, et al., Strabismus and diplopia in a patient with acute myeloid leukemia, Am. J. Case Rep. 15 (2014) 288–290.
[6] J. Buakhao, A. Tansawet, Cauda equina involvement in acute myeloid leukemia relapse, J. Med. Assoc. Thail. 94 (10) (2011) 1271–1275.
[7] I.K. Onal, A. Shorbagi, H. Göker, Y. Büyükasýk, L. Ozçakar, A. Tufan, et al., Cauda equina syndrome as a rare manifestation of leukemia relapse during post-allograft period, J. Natl. Med. Assoc. 98 (5) (2006) 808–810.
[8] C. Castagnola, A. Nozza, A. Corso, C. Bernasconi, The value of combination therapy in adult acute myeloid leukemia with central nervous system involvement, Haematologica 82 (5) (1997) 577–580.
[9] R. Holmes, M.J. Keating, A. Cork, Y. Broach, J. Trujillo, W.T. Dalton, et al., A

unique pattern of central nervous system leukemia in acute myelomonocytic leukemia associated with inv(16)(p13q22), Blood 65 (5) (1985) 1071–1078.
[10] C. Castagnola, A. Nozza, A. Corso, C. Bernasconi, The value of combination therapy in adult acute myeloid leukemia with central nervous system involvement, Haematologica 82 (5) (1997) 577–580.
[11] D. Martínez-Cuadrón, P. Montesinos, M. Pérez-Sirvent, A. Avaria, L. Cordón, R. Rodríguez-Veiga, et al., Central nervous system involvement at first relapse in patients with acute myeloid leukemia, Haematologica 96 (9) (2011) 1375–1379.