Cancer Treatment Communications 7 (2016) 17–20

Contents lists available at ScienceDirect

Cancer Treatment Communications

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

"Granulocytic sarcoma of cervical lymphnode: A diagnostic challenge"

Hemlata Das [a], Jagadish Hansa [b,*], Mahesh Chandra Sahu [b], Rabindra Nath Padhy [b]

[a] Department of Oncosciences, IMS & SUM Hospital, SOA University, Odisha, India
[b] Directorate of Medical Research, IMS & SUM Hospital, SOA University, Odisha, India

ARTICLE INFO

Article history:
Received 25 August 2015
Received in revised form
5 January 2016
Accepted 12 February 2016

Keywords:
Extramedullary acute myeloid leukemia
Immunohistochemistry
Myeloperoxidase

ABSTRACT

Introduction: Granulocytic sarcoma is an event associated with acute or chronic myeloid leukemia in which, the extramedullary site consists of myeloid blasts and/or immature myeloid cells. Primary granulocytic sarcoma becomes a diagnostic challenge especially in the absence of cited hematological disorder or when lymphnode becomes an extramedullary with remote co-incidence.
Presentation of case: This is a case of granulocytic sarcoma in a 15-year-old girl, who presented with a mass in the right side of neck, along with progressive dysphagia and aphasia. Histomorphologic diagnosis of the tissue was supported by immunohistochemical study with Avidin-biotin-peroxidase complex technique that was performed on formalin fixed tissue from the patient.
Discussion: The clinicopathologic diagnosis remains an elusive decision with a malignant lymphoma, because of the isolated cervical mass presentation. Moreover, the patient was hemodynamically stable without the presence of any leukemic blast cell in the peripheral blood.
Conclusion: Immunohistochemical study of the tissue from the neck mass helped to reach a correct diagnosis. The diagnosis was further reconfirmed on bone marrow trephine biopsy. A final trial with myeloid panel markers was the last alternatives to all differential diagnosis to round cell tumor. Tumor cells were immunoreactive to CD68, CD34, CD117 and myeloperoxidase, suggesting myeloid sarcoma.

1. Introduction

Granulocytic sarcoma (GS) is a neoplastic mass of immature myeloid cells (granulocytes) and/or monocytes at any extramedullary site such as, soft tissue or bone, producing a clinically evident tumor [1], with the eventual dysfunction of the organ/tissue. These tumors are often associated with acute myeloid leukemia (AML), chronic myeloid leukemia (CML), myeloproliferative and myelodysplastic disorders [2,3]. It may present either during the relapse or be the first sign of relapse itself or at relapses after allogeneic stem cell transplantation. The tumor may also be the initial manifestation of leukemia, as was in this case. It usually occurs either as an isolated or multiple lesion and may precede or coincide with AML in the bone marrow [1–3]. However, the occurrence of GS in cervical lymphnode or as lateral neck mass is rare [4–7]. Diagnostic confirmation usually requires immunophenotyping or immunohistochemical staining of the tissue. Often patients with GS without concomitant symptoms of leukemia are initially misdiagnosed [8]. We report a case of GS as a right lateral neck mass with dysphagia, aphasia and weight loss at the time of presentation.

2. Presentation of case

A 15 year old female presented in the Daycare unit of Institute of Medical Sciences and SUM Hospital with a neck mass on the right side and the chief complaint was difficulty in deglutition and speech. The mass was reported as reactive hyperplasia of lymphnode from fine needle aspiration cytology (FNAC), 6 months back. The mass had grown rapidly in the last month and she manifested with dysphagia, right side vocal cord paralysis and finally she developed aphasia.

At presentation, she was emaciated and the right cervical mass was tender and hard in consistency, measuring approximately 3×3 cm (Fig. 1). Computed tomography (CT) scan revealed a non-enhancing dense lesion in the retropharyngeal and paravertebral space extending from C3 to nasopharynx on the right side. Erosion of transverse process of C2 was also noted. Multiple enlarged necrotic parapharyngeal lymphnodes were seen along with a few level II nodes (Fig. 2A–C). But, paranasal sinuses, pterygomaxillary fossa, pterygopalatine foramen and buccal space were normal. Blood count, peripheral smear and liver function test results were within normal limits.

Incisional biopsy of the tumor revealed malignant small round cell tumor mimicking lymphoma cells. Immunohistochemical study was performed with CD45, CD20, CD3, myeloperoxidase, CD68, CD99 and desmin on the tumor tissue. Tumor cells were

* Corresponding author.
E-mail address: jagadish.hansa@gmail.com (J. Hansa).

http://dx.doi.org/10.1016/j.ctrc.2016.02.005
2213-0896/

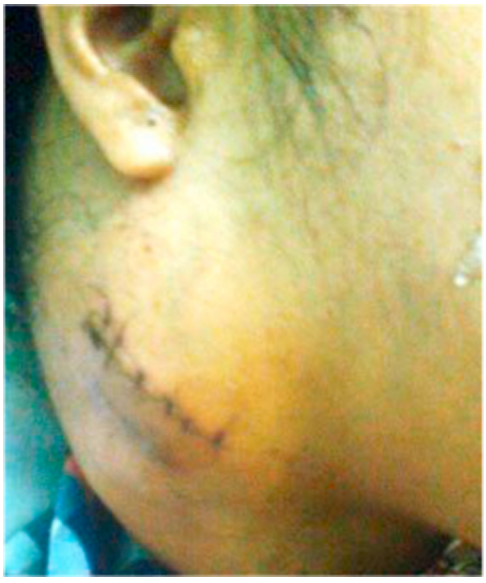

Fig. 1. Right lateral neck mass of the patient.

immunoreactive to myeloperoxidase enzyme (Fig. 3A) and CD68 (Fig. 3B), non-immunoreactive to lymphoma markers, CD99 and desmin. From these results, it was inferred as a malignant round cell tumor with minimal differentiation consistent with GS with a blastic variant.

Bone marrow aspiration showed 61% blast of which $<2\%$ were positive for Sudan Black B. A marrow trephine biopsy revealed a cellularity of 90–100% being replaced by sheets of medium to large sized myeloblasts with moderate granular cytoplasm (Fig. 4A–C). These cells had immunoreactive score of 3+ with myeloperoxidase (Fig. 4D), 1+ for CD68 and CD117, but negative for CD34. Scattered islands of myeloid and erythroid cells were present, but no megakaryocytes were found in the section. It was thus inferred as an AML without differentiation and the bone marrow study too corroborated the soft tissue diagnosis as GS.

To manage her local symptoms, she was treated with 1500 cGy radiotherapy over 4 fractions. Her general condition was deteriorated due to progressive dysphagia, followed by the massive pneumonic consolidation in bilateral lungs. Her hematological parameters subsequently presented a picture of bicytopenia (anemia and thrombocytopenia), but still no atypical cell was found in the peripheral blood. Palliative measures with Ryle's tube feeding, transfusions and the antibiotic stewardship were undertaken, but gradually her general condition became worst with complications of pneumonia and she passed away in respiratory failure.

3. Discussion

Myeloid leukemia is a systemic disease affecting both hematological system and extra-medullary tissue alike, characterized by uncontrolled proliferation of immature abnormal cells of myeloid lineage [9]. But GS is a clinicopathological entity defined by solid, localized tumor mass due to extramedullary proliferation of blasts or immature precursors of granulocytes involving one or more of the myeloid lineages. The normal architecture of the involved tissue is disrupted partially or completely in GS and is often associated with malignant hematopoietic diseases, viz., AML, CML, myeloproliferative and myelodysplastic disorders. GS is a rare entity and has also been addressed as myeloid sarcoma (MS), myeloblastoma and extramedullary myeloid cell tumor [10]. A localized MS presenting before the onset of systemic leukemic disease has been termed as the 'primary MS' [9]. In such cases, the diagnosis could be challenging, especially, if it was not preceded by leukemia or any other bone marrow disease. It can be the initial manifestation of a disease in approximately a half of patients, although bone marrow examination usually shows evidence of hematological disorders. Indeed, GS might have occurred *de novo,* but this case might also represent a relapse of leukemia or might be an acute blastic transformation of a myelodysplastic syndrome [11]. It usually occurs either as an isolated lesion and may precede or coincide with AML in the bone marrow.

MS has a predilection for males (1.2:1), but there is no apparent age preference. MS has been reported in 2.5–9.1% of cases of patients with AML, although these sarcomas are likely under diagnosed [12]. Cheng et al. concluded that the survival rate of MS is only 30.8%. The tumor can involve any part of the body, but commonly involved sites include subperiosteal bone structures of the skull, paranasal sinuses, sternum, ribs, vertebrae, pelvis; soft tissue, testis, bone/spine, lymph nodes and skin [2,13] and less often the central nervous system, gastrointestinal tract and the orbits. The head and neck region is affected in 12–43% of cases [14]. Radiologically, GS may mimic lymphomas due to the uniform contrast enhancement on CT scan.

It is frequently mistaken for non-Hodgkin lymphoma (NHL), small round cell tumor (neuroblastoma, rhabdomyosarcoma, Ewing sarcoma/remitive neuroendocrine tumor (PNET), and medulloblastoma) and undifferentiated carcinoma. The diagnosis is missed in about 50% of cases when immunohistochemistry is not used [2] and the most common suggested diagnosis is that of a NHL. 46–75% of patients with isolated MS are initially diagnosed with other conditions such as NHL [15]. As it is known, 10 of 25 cases of *de novo* MS were initially diagnosed as diffuse large B-cell lymphoma, small lymphocytic lymphoma, peripheral T-cell lymphoma, T-cell precursor lymphoma and myeloid metaplasia when adequate immunohistochemistry studies were not performed [2]. Therefore selecting a panel of markers needs a list of differentials

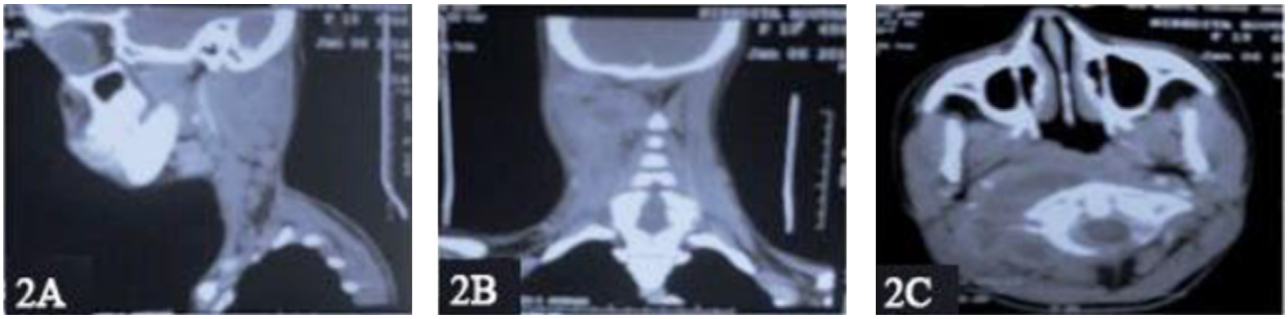

Fig. 2. 2A – CT scan lateral view, 2B – CT Scan Postero Anterior view, 2C – CT scan Transverse view. The level of cervical mass CT scan of the patient showing different views (sagittal and transverse cross-sectional image of the neck shows a non-enhancing dense lesion in the retropharyngeal and paravertebral space on right side with erosion of transverse process of c2 and multiple enlarged, necrotic parapharyngeal lymphnode along with few level II nodes).

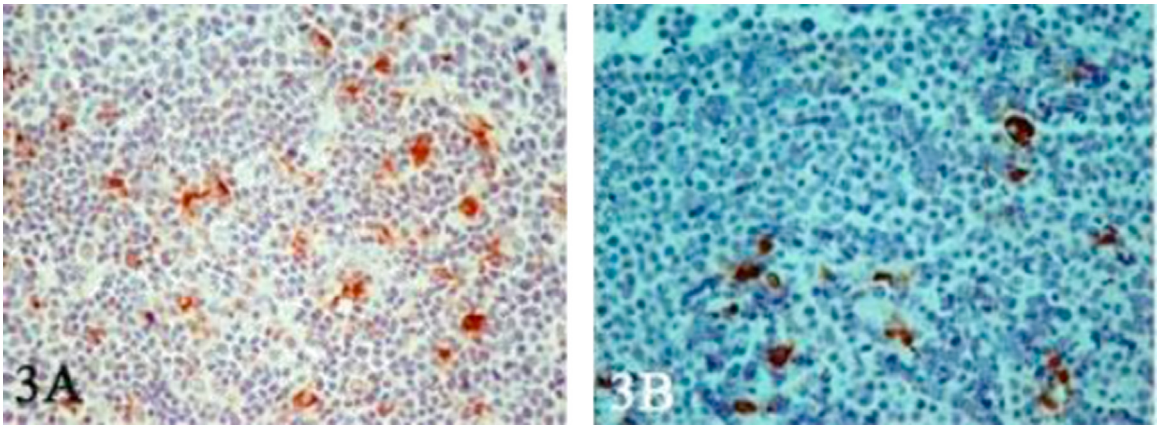

Fig. 3. A – IHC of the tumor tissue showing positivity with myeloperoxidase, B – IHC of the tumor tissue showing positivity with CD68. Microscopic view of the tumor showing uniform looking malignant small round cell mimicking morphologically as lymphoma.

of round cell tumor, including the myeloid markers.

In this case, there was absence of the clue of hematological disorder, i.e., total cell count; and the cell morphology in peripheral smear was absolutely within normal limits. The diagnosis and treatment was a challenge in itself for the clinician and the pathologist. Moreover, the site of the mass made it further complicated. Without immunohistochemistry, it was a critical task to differentiate blastic type of GS from malignant lymphomas and other small round cell tumors from its morphological study. Therefore a panel of marker was selected, which included the list of differentials of round cell tumor, including the myeloid markers, the later turned out to be positive. Thus, immunohistochemistry offers one of the best methods in establishing the diagnosis of GS [2]. Positive staining for markers MPO, CD34, CD117, and CD68 and lysozyme help identify the myeloid neoplastic cells [16,17].

4. Conclusion

GS or MS in cervical lymphnode is a rare extramedullary manifestation of AML. A high index of suspicion is required for diagnosing it. Therefore the entity needs to be remembered in the differential diagnosis of poorly differentiated tumors involving the head and neck region, which can be differentiated on the basis of immunohistochemistry.

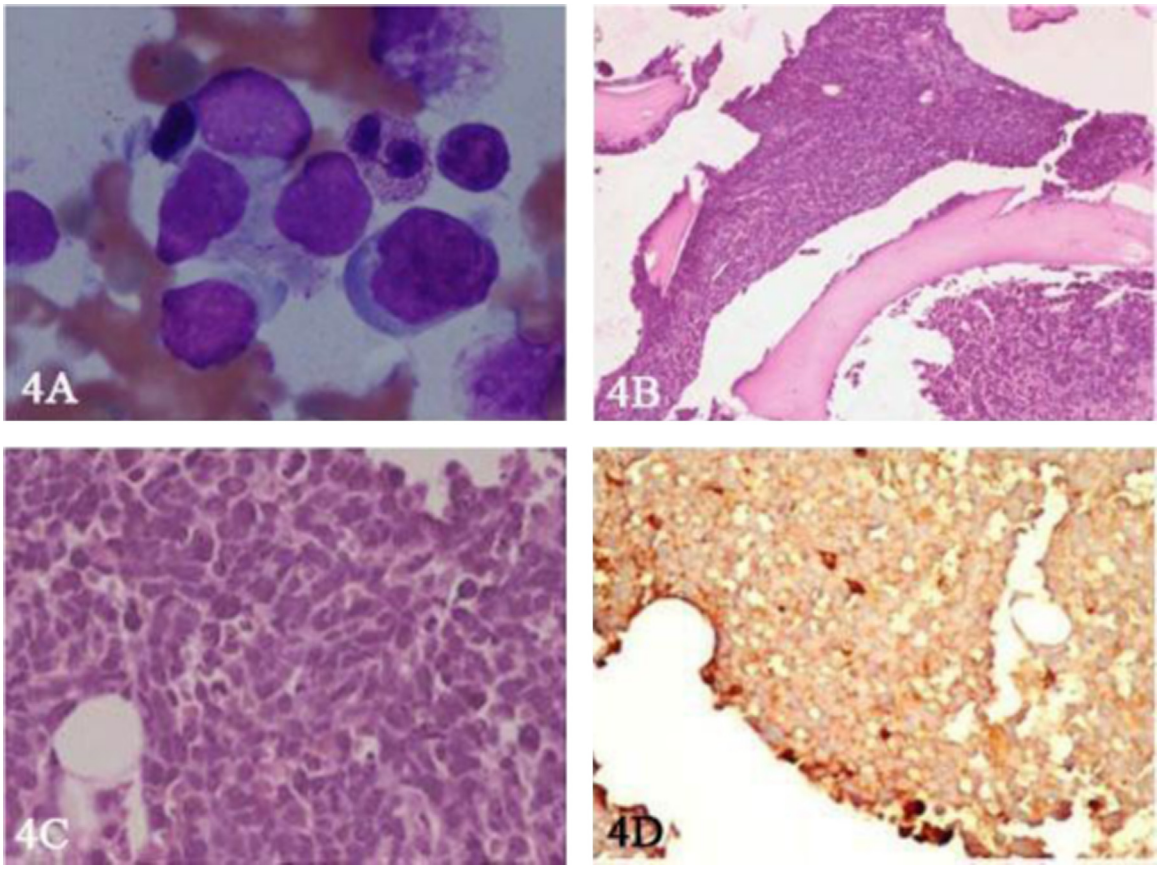

Fig. 4. 4A – Bone marrow aspirating showing myeloblast, 4B – Bone marrow trephine biopsy (40x) showing high cellularity with myeloid precursor, 4C – High power view of bone marrow trephine biopsy showing myeloid precursor, 4D – IHC on marrow trephine biopsy showing positivity with myeloperoxidase.

Conflict of interest

All authors declare none to conflict.

Consent of patient

The patient consented for his case to be in publication as case report on March 2015.

Acknowledgment

All authors acknowledge from the bottom of the heart to Somadatta Das for his contribution to the artwork of the manuscript and also to the staff of Department of Pathology for their immense help regarding diagnosis of the disease.

References

[1] A.F. Yilmaz, G. Saydam, F. Sahin, Y. Baran, Granulocytic sarcoma: a systematic review, Am. J. Blood Res. 3 (4) (2013) 265–270.
[2] S.A. Pileri, S. Ascani, M.C. Cox, C. Campidelli, F. Bacci, M. Piccioli, et al., Myeloid sarcoma: clinico-pathologic, phenotypic and cytogenetic analysis of 92 adult patients, Leukemia 21 (2) (2007) 340–350, http://dx.doi.org/10.1038/sj.leu.2404491.
[3] C. Campidelli, C. Agostinelli, R. Stitson, S.A. Pileri, Myeloid sarcoma: extramedullary manifestation of myeloid disorders, Am. J. Clin. Pathol. 132 (3) (2009) 426–437, http://dx.doi.org/10.1309/AJCP1ZA7HYZKAZHS.
[4] S.B. An, J.E. Cheon, I.O. Kim, W.S. Kim, H.S. Ahn, H.Y. Shin, et al., Granulocytic sarcoma presenting with necrotic cervical lymph nodes as an initial manifestation of childhood leukaemia: imaging features, Pediatr. Radiol. 38 (6) (2008) 685–687, http://dx.doi.org/10.1007/s00247-008-0748-6.
[5] Y.H. Lee, N.J. Lee, E.J. Choi, J.H. Kim, Granulocytic sarcoma (chloroma) presenting as a lateral neck mass: initial manifestation of leukemia: a case report, Eur. Arch. Otorhinolaryngol. 263 (1) (2006) 16–18, http://dx.doi.org/10.1007/s00405-005-0952-z.
[6] O. Dikbas, M. Isik, T. Purnak, O. Karadag, A. Uner, K. Altundag, Isolated granulocytic sarcoma of the head and neck preceding acute myeloid leukemia, Am. J. Hematol. 76 (1) (2004) 95–96, http://dx.doi.org/10.1002/ajh.20021.
[7] T. Imamura, S. Matsuo, T. Yoshihara, T. Chiyonobu, K. Mori, H. Ishida, et al., 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) (2004) 186–189, http://dx.doi.org/10.1532/IJH97.04040.
[8] M. Breccia, F. Mandelli F, M.C. Petti, M. D'Andrea, E. Pescarmona, S.A. Pileri, et al., Clinico-pathological characteristics of myeloid sarcoma at diagnosis and during follow-up: report of 12 cases from a single institution, Leuk. Res. 28 (11) (2004) 1165–1169, http://dx.doi.org/10.1016/j.leukres.2004.01.022.
[9] D. Pan, Y. Tay, S. Appu, M. Frydenberg, Primary myeloid sarcoma of urinary bladder, Internet J. Urol. 8 (2) (2010) 1–3.
[10] M.J. Roth, L.J. Medeiros, K. Elenitoba-Johnson, M. Kuchnio, E.S. Jaffe, M. Stetler-Stevenson, Extramedullary myeloid cell tumors. An immunohistochemical study of 29 cases using routinely fixed and processed paraffin-embedded tissue sections, Arch. Pathol. Lab. Med. 119 (9) (1995) 790–798.
[11] R. Alrumaih, M. Saleem, S. Velagapudi, M.A. Dababo, Lateral pharyngeal wall myeloid sarcoma as a relapse of acute biphenotypic leukemia: a case report and review of the literature, J. Med. Case Rep. 7 (2013) 292, http://dx.doi.org/10.1186/1752-1947-7-292.
[12] S. Nandedkar, M. Kawatra, K. Malukani, Myeloid sarcoma de novo presenting as generalized lymphadenopathy, Clin. Cancer Investig. J. 2 (1) (2013) 86–89, http://dx.doi.org/10.4103/2278-0513.110815.
[13] R.D. Brunnung, E. Matutes, G. Flandrin, J. Vardiman, J. Bennett, D. Head D, et al., Acute Myeloid Leukemias, in: E.S. Jaffe, et al., (Eds.), World Health Organization Classification of Tumors. Pathology and Genetics of Tumours of Haematopoietic and Lymphoid Tissue, IARC Press, Lyon, France, 2001, pp. 77–105.
[14] R.S. Neiman, M. Barcos, C. Berard, H. Bonner, R. Mann, R.E. Rydell, et al., Granulocytic sarcoma: a clinicopathologic study of 61 biopsied cases, Cancer 48 (6) (1981) 1426–1437.
[15] P. Narayan, V. Murthy, M. Su, R. Woel, I.R. Grossman, R.S. Chamberlain, Primary myeloid sarcoma masquerading as an obstructing duodenal carcinoma, Case Rep. Hematol. 2012 (2012) 1–7, http://dx.doi.org/10.1155/2012/490438.
[16] E. Derenzini, S. Paolini, G. Martinelli, C. Campidelli, G.L. Grazi, C. Calabrese, et al., Extramedullary myeloid tumour of the stomach and duodenum presenting without acute myeloblastic leukemia: a diagnostic and therapeutic challenge, Leuk. Lymphoma 49 (1) (2008) 159–162, http://dx.doi.org/10.1080/10428190701704621.
[17] R.L. Bakst, M.S. Tallman, D. Douer, J. Yahalom, How I treat extramedullary acute myeloid leukemia, Blood 118 (14) (2011) 3785–3793, http://dx.doi.org/10.1182/blood-2011-04-347229.