Annals of Hematology (2019) 98:2825–2827
https://doi.org/10.1007/s00277-019-03828-2

LETTER TO THE EDITOR

Aggressive systemic mastocytosis: a diagnostic challenge in a patient with myotonic dystrophy type 2: a case report

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Received: 29 May 2019 / Accepted: 21 October 2019 / Published online: 9 November 2019

Dear Editor,

Systemic mastocytosis (SM) is a neoplastic disease of mast cells (MCs) with heterogeneous clinical presentations, and is often overlooked [1, 2]. The spectrum ranges from indolent to aggressive forms [3, 4].

A 55-year-old woman with known familial myotonic dystrophy type 2 (DM2) proven by CCTG-repeat expansion in the *ZNF9* gene was referred with a diagnosis of unclassified myeloproliferative neoplasm with 10% bone marrow (BM) blasts and *KRAS*, *ASXL1*, and *RUNX1* mutations. Over two months, she complained of weight loss, fever, and worsening of her neurological symptoms (muscle weakness/dysphagia). Enteral nutrition by percutaneous endoscopic gastrostomy tube (PEG) was initiated.

A body mass index (BMI) of 13.6 kg/m^2, normal skin, and hepatosplenomegaly were seen. Hilar lymphadenopathy was detected by CT scan. Laboratory analysis showed hypoalbuminemia, elevated lactate dehydrogenase, Hb 4.4 g/dl, platelets 78 × 10^9/L, and WBC 39.80 × 10^9/L with a left shift without eosinophilia, monocytosis, or blasts.

Rapid neurological deterioration is unusual for DM2, which is usually associated with a good prognosis [5].

Assessment of serum tryptase as part of our routine workup for hematologic diseases was 46.9 μg/L (reference range < 11 μg/L). A repeat BM biopsy revealed a hypercellular marrow with delayed myelopoietic maturation and normal blast count (Fig. 1a, b). Therein, CD2+, CD25+, CD117+, and MC tryptase-positive multifocal dense infiltrates of MCs (20/cluster) were detected (Fig. 1c). An associated hematological neoplasm was histopathologically excluded. We speculate that MCs were initially misinterpreted as blasts. Cytogenetics were normal but the activating mutation *KIT*D816V was present.

A diagnosis of SM could be made based on the major criterion (≥ 15 MC in clusters) and three minor criteria (*KIT* mutation, CD25/CD2 co-expression, serum tryptase > 20 μg/L). Due to the presence of C-findings (transfusion-dependent anemia, splenomegaly with thrombocytopenia, and malabsorption with weight loss), the criteria for aggressive SM (ASM) were fulfilled [1]. A hilar lymph node biopsy revealed small lymphocytes (Fig. 1d, e) next to dense blastoid cell infiltrates of myeloid lineage without MCs consistent with extramedullary hematopoiesis (Fig. 1f–h).

Together with the neurologist, we hypothesized that ASM and not the natural course of DM2 was causative for the rapid neurological deterioration. Treatment with the KIT tyrosine kinase inhibitor midostaurin was initiated. Within three

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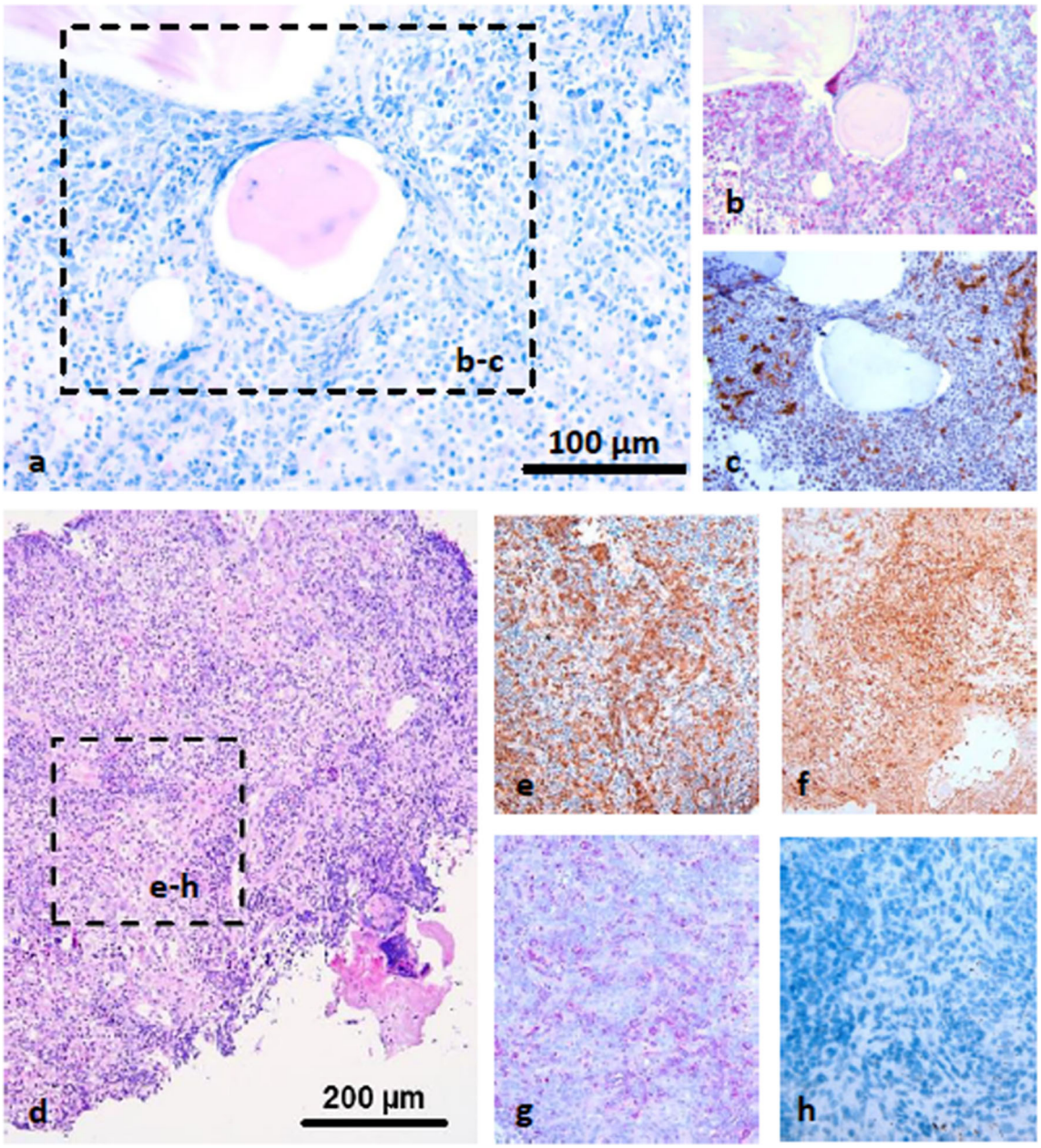

Fig. 1 **a** Bone marrow: Giemsa. **b** Bone marrow: Chloracetate esterase. **c** Bone marrow: Mast cell tryptase. **d** Hilar lymph node: Hematoxylin and eosin staining. **e** Hilar lymph node: CD 20. **f** Hilar lymph node: Myeloperoxidase. **g** Hilar lymph node: Chloracetate esterase. **h** Hilar lymph node: CD 34

months, the patient gained weight, regained muscle power, dysphagia disappeared, and the PEG was removed. Although unusual [6], the blood count normalized (Hb 13.6 g/dl, platelets 170 × 10^9/L, WBC 5 × 10^9/L with a normal differential) and hilar lymphadenopathy decreased. Serum tryptase and BM-MCs were unchanged. A pure clinical response was achieved [7].

Because of the slow progressive course of DM2 and the poor prognosis of ASM (particularly in the presence of KIT-independent oncogenic driver mutations), a consensus for allogeneic hematopoietic cell transplantation (HCT) was made on a risk-benefit base [5, 8]. To our knowledge, this is the first report of a patient with DM2 and ASM. The impact of HCT on DM2 is unknown.

In summary, awareness of physicians to SM as a possibility in the differential diagnosis of unclear clinical scenarios is the first step to make the diagnosis and offer adequate therapy. Serum tryptase is a simple tool that could draw the attention to SM.

Compliance with ethical standards

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

Informed consent The patient has given her informed consent for each diagnostic and therapeutic step presented in this case report as part of the routine clinical work up.

Abbreviations ASM, aggressive systemic mastocytosis; BM, bone marrow; BMI, body mass index; CT scan, computed tomography scan; DM2, myotonic dystrophy type 2; Hb, hemoglobin; HCT, hematopoietic cell transplantation; MCs, mast cells; MPN, myeloproliferative neoplasm; PEG, percutaneous endoscopic gastrostomy tube; SM, systemic mastocytosis; WBC, white blood count

References

1. Valent P, Akin C, Metcalfe DD (2017) Mastocytosis: 2016 updated WHO classification and novel emerging treatment concepts. Blood 129:11
2. Horny HP, Valent P (2001) Diagnosis of mastocytosis: general histopathological aspects, morphological criteria, and immunohistochemical findings. Leuk Res 25:7
3. Pardanani A (2013) Systemic mastocytosis in adults: 2013 update on diagnosis, risk stratification, and management: Annual Clinical Updates in Hematological Malignancies: A Continuing Medical Education Series. Am J Hematol 88:7
4. Swerdlow SH, Campo E, Harris NL et al (2017) WHO classification of tumours of haematopoietic and lymphoid tissues. Revised, 4th edn. International Agency for Research on Cancer, Lyon
5. Schoser B, Timchenko L (2010) Myotonic dystrophies 1 and 2: complex diseases with complex mechanisms. Curr Genomics 11(2):77–90
6. Gotlib J, Kluin-Nelemans HC, George TI, Akin C, Sotlar K, Hermine O, Awan FT, Hexner E, Mauro MJ, Sternberg DW, Villeneuve M, Huntsman Labed A, Stanek EJ, Hartmann K, Horny HP, Valent P, Reiter A (2016) Efficacy and safety of midostaurin in advanced systemic mastocytosis. N Engl J Med 374:2530–2541
7. Valent P, Akin C, Escribano L, Födinger M, Hartmann K, Brockow K, Castells M, Sperr WR, Kluin-Nelemans HC, Hamdy NA, Lortholary O, Robyn J, van Doormaal J, Sotlar K, Hauswirth AW, Arock M, Hermine O, Hellmann A, Triggiani M, Niedoszytko M, Schwartz LB, Orfao A, Horny HP, Metcalfe DD (2007) Standards and standardization in mastocytosis: consensus statements on diagnostics, treatment recommendations and response criteria. Eur J Clin Investig 37:435–453
8. Jawhar M, Schwaab J, Schnittger S, Meggendorfer M, Pfirrmann M, Sotlar K, Horny HP, Metzgeroth G, Kluger S, Naumann N, Haferlach C, Haferlach T, Valent P, Hofmann WK, Fabarius A, Cross NC, Reiter A (2016) Additional mutations in *SRSF2*, *ASXL1* and/or *RUNX1* identify a high-risk group of patients with *KIT* D816V+ advanced systemic mastocytosis. Leukemia 30:136–143