



Paraneoplastic pemphigus associated with systemic mastocytosis

Lydia Rosalind Joy Eccersley, a Victor Hoffbrand, Malcolm H.A. Rustin,
Chris Mcnamara

► To cite this version:

Lydia Rosalind Joy Eccersley, a Victor Hoffbrand, Malcolm H.A. Rustin, Chris Mcnamara. Paraneoplastic pemphigus associated with systemic mastocytosis. American Journal of Hematology, 2009, 84 (12), pp.847-n/a. 10.1002/ajh.21462 . hal-00486847

HAL Id: hal-00486847

<https://hal.science/hal-00486847>

Submitted on 27 May 2010

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American Journal of Hematology

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Journal:	<i>American Journal of Hematology</i>
Manuscript ID:	AJH-09-0346
Wiley - Manuscript type:	Images in Hematology
Date Submitted by the Author:	18-May-2009
Complete List of Authors:	Eccersley, Lydia; Royal Free Hospital, Haematology Hoffbrand, A; Royal Free Hospital, Haematology Rustin, Malcolm; Royal Free Hospital, Dermatology McNamara, Chris; Royal Free Hospital, Haematology
Keywords:	Neoplasia- myeloid leukemias and dysplasias, Pathology



Paraneoplastic pemphigus associated with systemic mastocytosis

LRJ Eccersley, MA, MRCP, DTM&H, Specialist Registrar in Haematology, Royal Free Hospital, London, UK, lydia.eccersley@nhs.net (submitting author)

AV Hoffbrand, MA, FRCP, DM, FRCPath, DSc, FMEDSci, Emeritus Professor of Haematology, Royal Free and University College Medical School, London, U.K. v.hoffbrand@rfc.ucl.ac.uk

MHA Rustin, BSc, MD, FRCP, Consultant Dermatologist, Royal Free Hospital, London, U.K. malcolmrustin@btinternet.com

C J McNamara, FRACP, FRCPA, Consultant Haematologist, Royal Free Hospital, London, U.K. Christopher.Mcnamara@royalfree.nhs.uk (corresponding author)

Corresponding author: Dr. C J McNamara, FRACP, FRCPA, Consultant Haematologist, Royal Free Hospital, Pond Street, London, NW3 2QG U.K.

Phone: 020 7794 0500 ext. 33260

Fax: 020 7830 2092

e-mail: Christopher.Mcnamara@royalfree.nhs.uk

Word count: 431

Number of tables: 0

Number of figures: 5

Short running title: Paraneoplastic pemphigus associated with systemic mastocytosis

Keywords: Paraneoplastic pemphigus, mastocytosis, pathology

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3 A 50-year-old man presented in 1996 with a pigmented papular eruption on his limbs
4 which urticated on rubbing. Histology confirmed the diagnosis of urticaria
5 pigmentosa. Over the next two years he developed hepatosplenomegaly and a raised
6 serum tryptase. Attempted bone marrow aspiration yielded a dry tap, and trephine
7 biopsy showed a hypercellular marrow with a diffuse infiltrate of mast cells with
8 round to spindle-shaped nuclei, positive for mast cell tryptase, CD117 and CD25.
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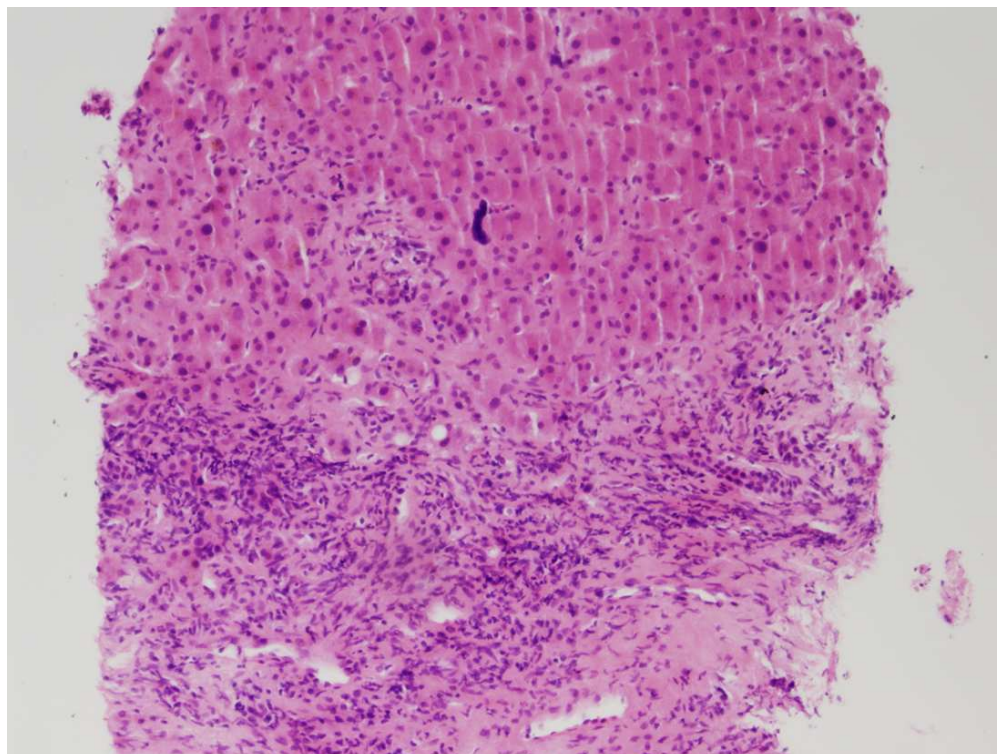
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20 In 1998, progressive anemia led to treatment with interferon alpha, but this failed to
21 improve either his hemoglobin or his symptoms. In 2000, hydroxycarbamide led to a
22 reduction in organomegaly, at the expense of worsening anemia. He then had
23 improvement in anemia, reduction in size of liver and spleen and some symptomatic
24 improvement with 2-chlorodeoxyadenosine; he received a total of four courses over
25 an eight-month period from 2001-2002. In 2006 he developed ascites in addition to
26 increasing hepatosplenomegaly. Liver biopsy showed a nodular architecture with
27 widespread septal and parenchymal mast cell infiltration, again CD117 and mast cell
28 tryptase positive, (Figures 1A-D), consistent with cirrhosis due to mastocytosis.
29 Biopsy of enlarged lymph nodes in the abdomen showed only systemic mastocytosis
30 and no other tumor. Molecular studies identified the *c-kit* D816V mutation, which is
31 known to be present in at least 95% of cases of systemic mastocytosis when sensitive
32 detection methods are used. At this stage he failed to respond to further 2-
33 chlorodeoxyadenosine.
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55 In December 2007 he developed severe erosive mucositis affecting the soft palate and
56 lips, a widespread urticated and lichenoid eruption and subsequently a severe
57 blistering rash covering over 80% of the body surface. A diagnosis of paraneoplastic
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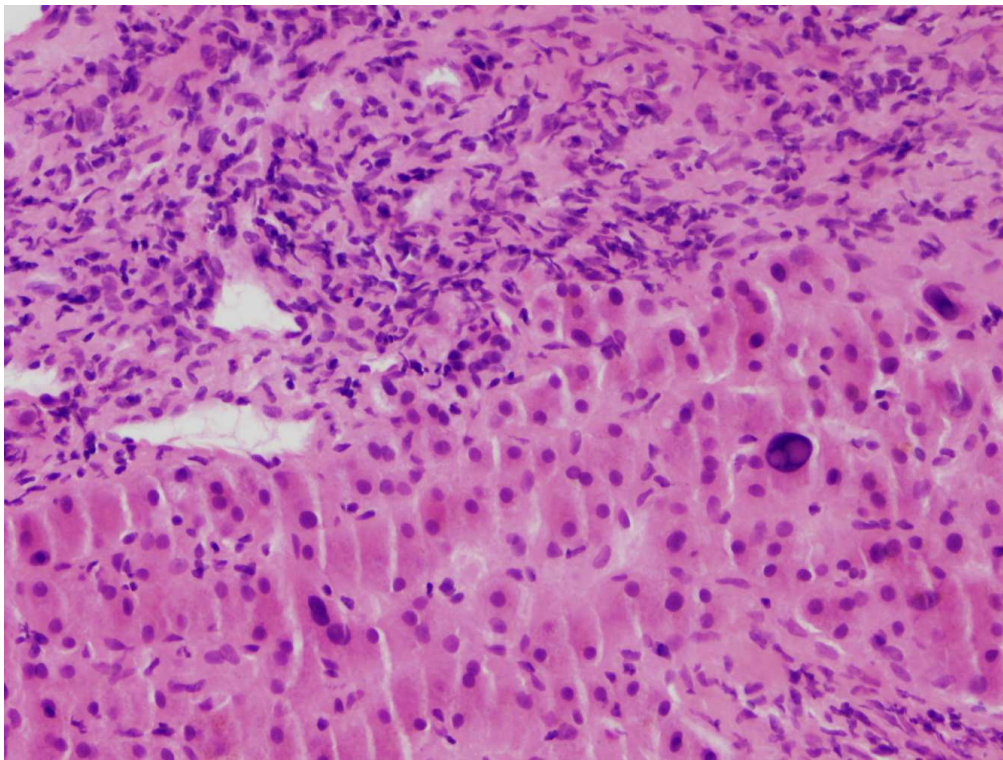
pemphigus (PNP) (figure 2) was confirmed by direct and indirect immunofluorescence with intercellular IgG antibodies detected on monkey esophagus to a titre of 1/400 and positive staining on rat bladder at a titre of 1/200. The rash failed to improve with high-dose prednisone (60mg/day), high dose intravenous immunoglobulin (2g/kg) repeated every three weeks for a total of four courses, and rituximab 375mg/m². Deoxycoformycin and nilotinib were also tried over a ten-week period, in an attempt to control the underlying mastocytosis and hence the PNP, without benefit; the patient's clinical condition deteriorated and he subsequently died.

PNP is typically associated with lymphoproliferative disorders; however, it has not to our knowledge been previously associated with systemic mastocytosis. The treatment of PNP involves treating the underlying condition, as well as the use of immunosuppressive agents, rituximab or intravenous immunoglobulin; the success of these agents is variable. Unfortunately in this case neither the PNP nor the underlying mastocytosis responded to multiple lines of therapy.



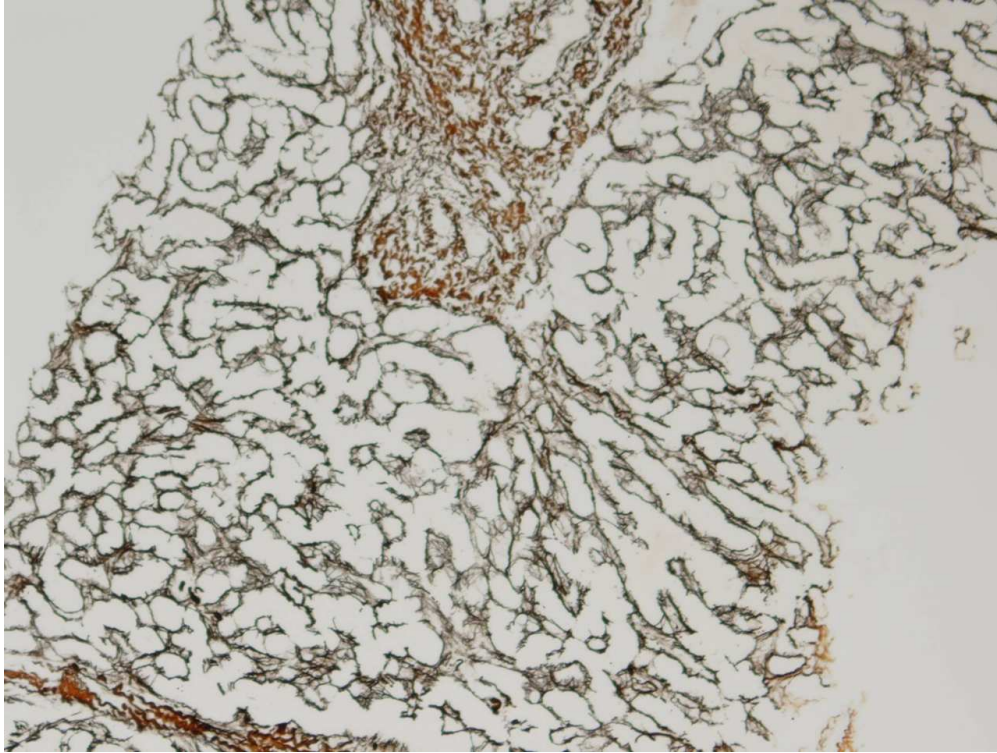
Liver biopsy: haematoxylin and eosin (H&E) stain, demonstrating liver architecture distorted by an infiltrate of spindle-shaped mast cells (x100)
185x140mm (150 x 150 DPI)

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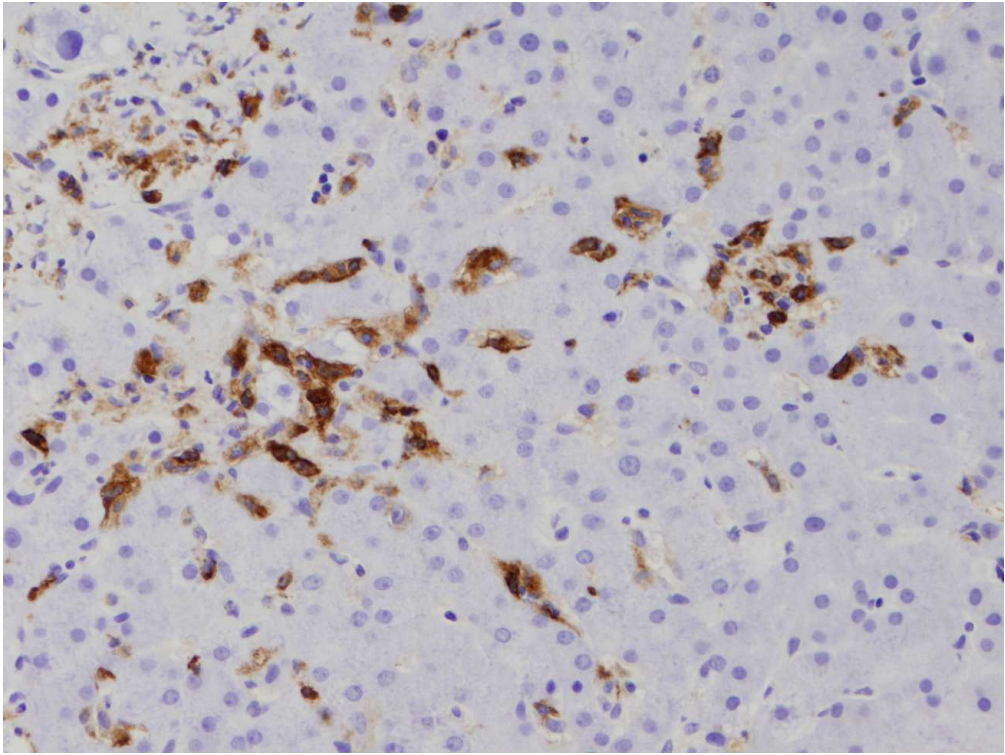


Liver biopsy: H&E stain (x200)
225x170mm (150 x 150 DPI)

Review



Liver biopsy: silver stain demonstrating reticulin fibrosis (x 100)
217x163mm (150 x 150 DPI)



Liver biopsy: mast cell tryptase (x200)
220x166mm (150 x 150 DPI)



Widespread bullous and erythema multiforme-like lesions
123x185mm (123 x 123 DPI)