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Paraneoplastic pemphigus associated with systemic mastocytosis

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Paraneoplastic pemphigus associated with systemic mastocytosis

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Paraneoplastic pemphigus associated with systemic mastocytosis

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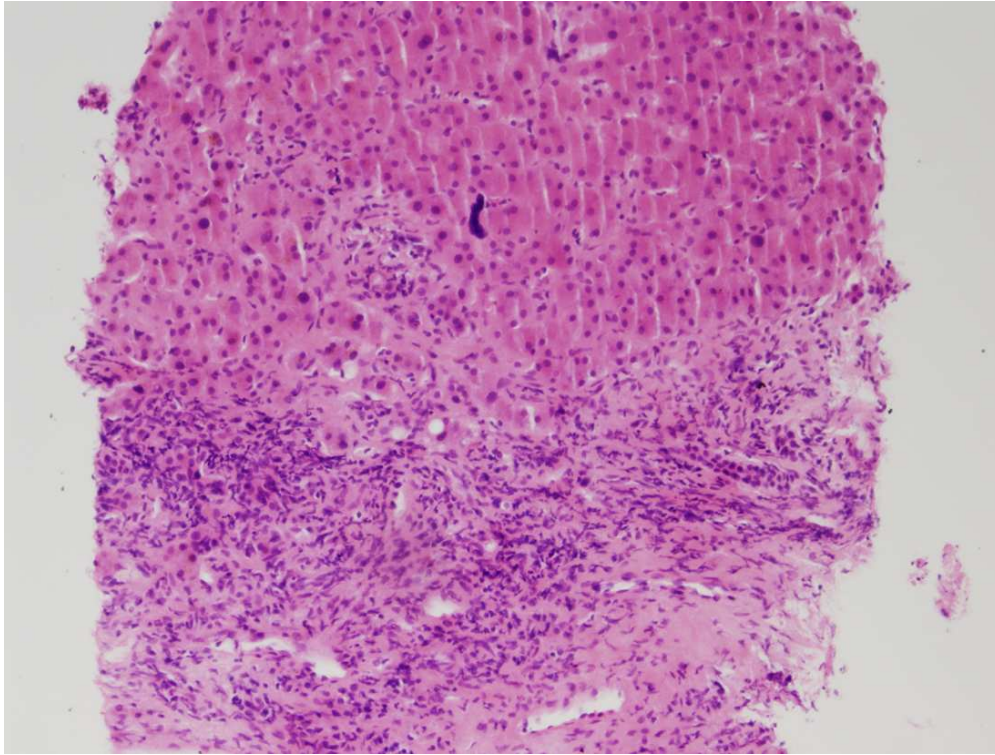
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3 A 50-year-old man presented in 1996 with a pigmented papular eruption on his limbs
4 which urticated on rubbing. Histology confirmed the diagnosis of urticaria
5 pigmentosa. Over the next two years he developed hepatosplenomegaly and a raised
6 serum 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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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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3 pemphigus (PNP) (figure 2) was confirmed by direct and indirect
4 immunofluorescence with intercellular IgG antibodies detected on monkey esophagus
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8 to a titre of 1/400 and positive staining on rat bladder at a titre of 1/200. The rash
9
10 failed to improve with high-dose prednisone (60mg/day), high dose intravenous
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12 immunoglobulin (2g/kg) repeated every three weeks for a total of four courses, and
13
14 rituximab 375mg/m². Deoxycoformycin and nilotinib were also tried over a ten-week
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17 period, in an attempt to control the underlying mastocytosis and hence the PNP,
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20 without benefit; the patient's clinical condition deteriorated and he subsequently died.
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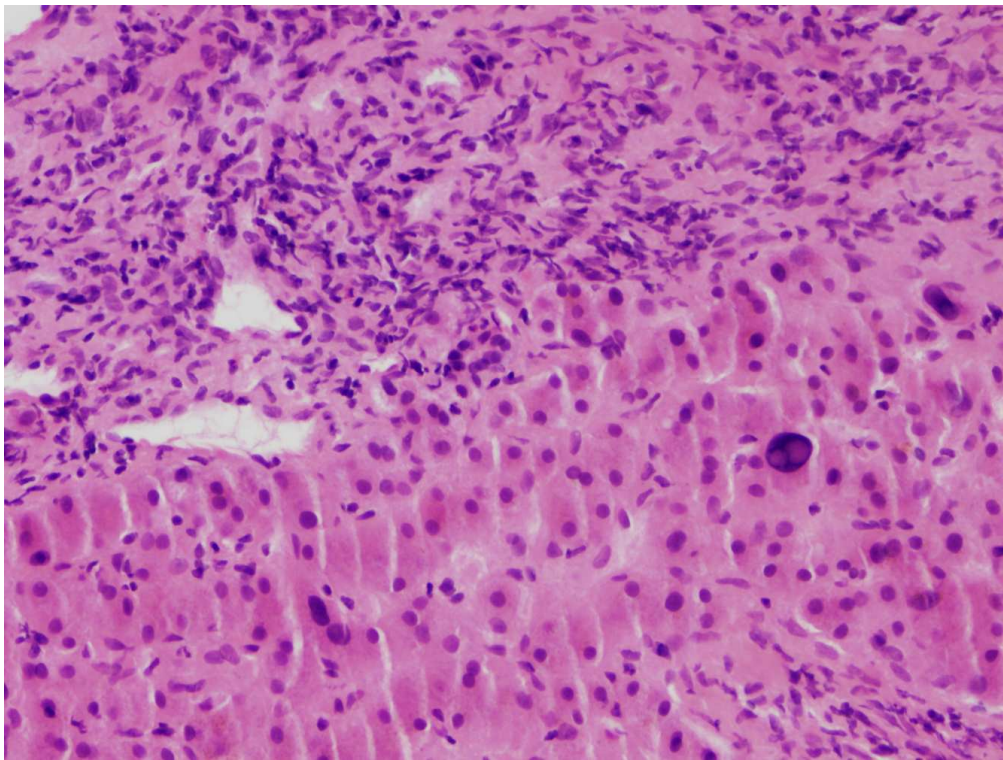
24 PNP is typically associated with lymphoproliferative disorders; however, it has not to
25
26 our knowledge been previously associated with systemic mastocytosis. The treatment
27
28 of PNP involves treating the underlying condition, as well as the use of
29
30 immunosuppressive agents, rituximab or intravenous immunoglobulin; the success of
31
32 these agents is variable. Unfortunately in this case neither the PNP nor the underlying
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34 mastocytosis responded to multiple lines of therapy.
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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)

Review

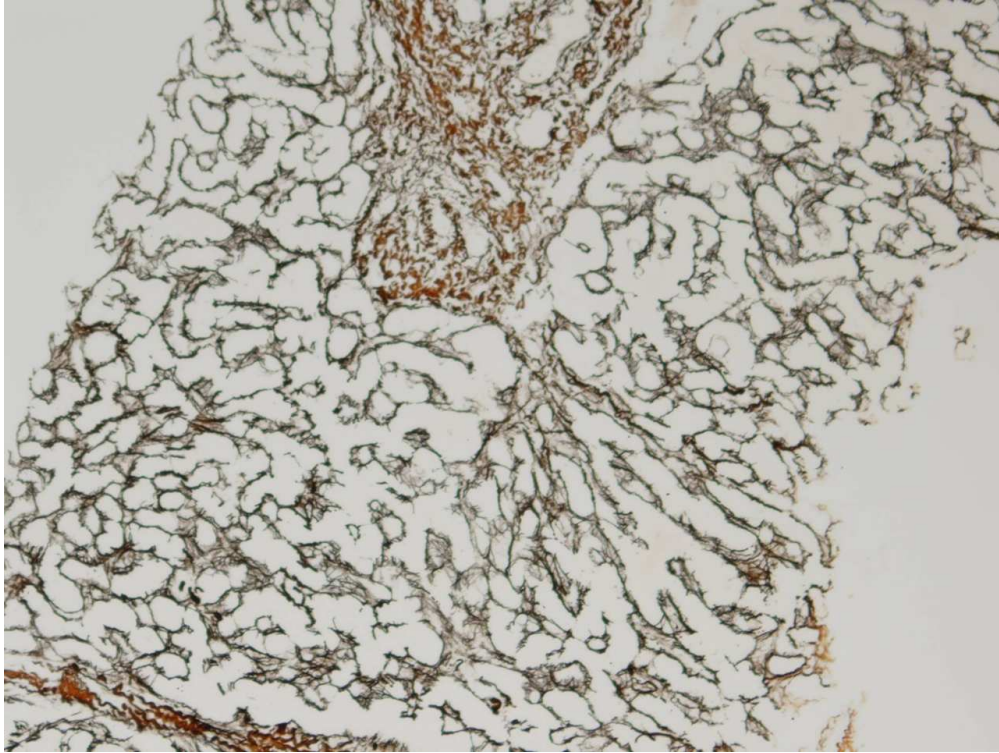
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Liver biopsy: H&E stain (x200)
225x170mm (150 x 150 DPI)

Review

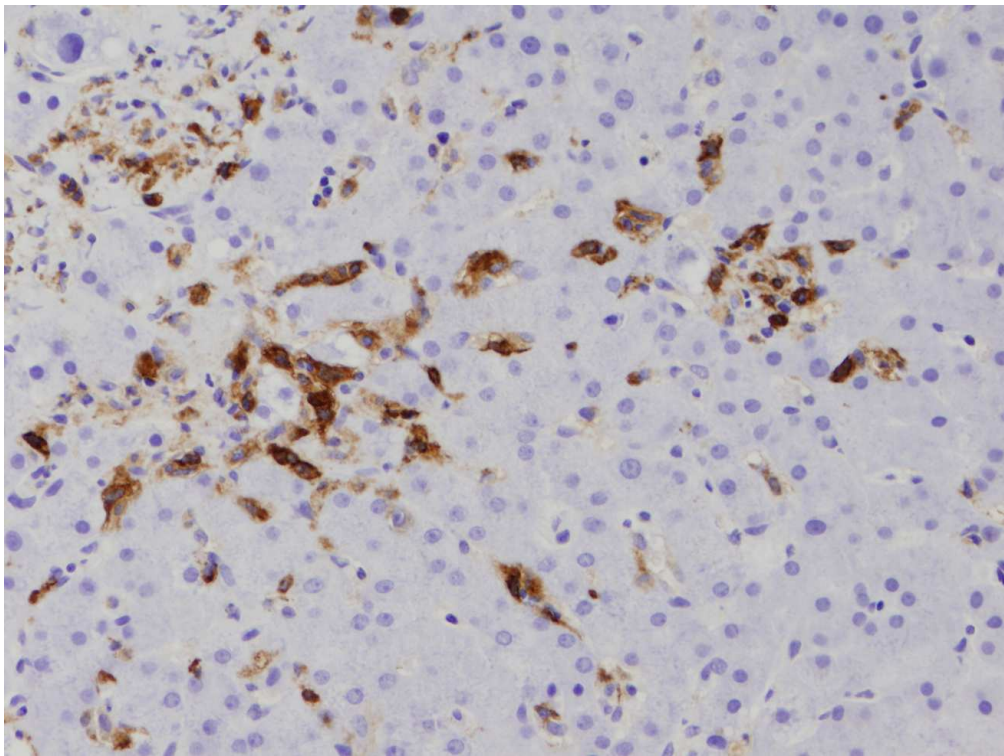
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Liver biopsy: silver stain demonstrating reticulin fibrosis (x 100)
217x163mm (150 x 150 DPI)

Review

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

Review

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