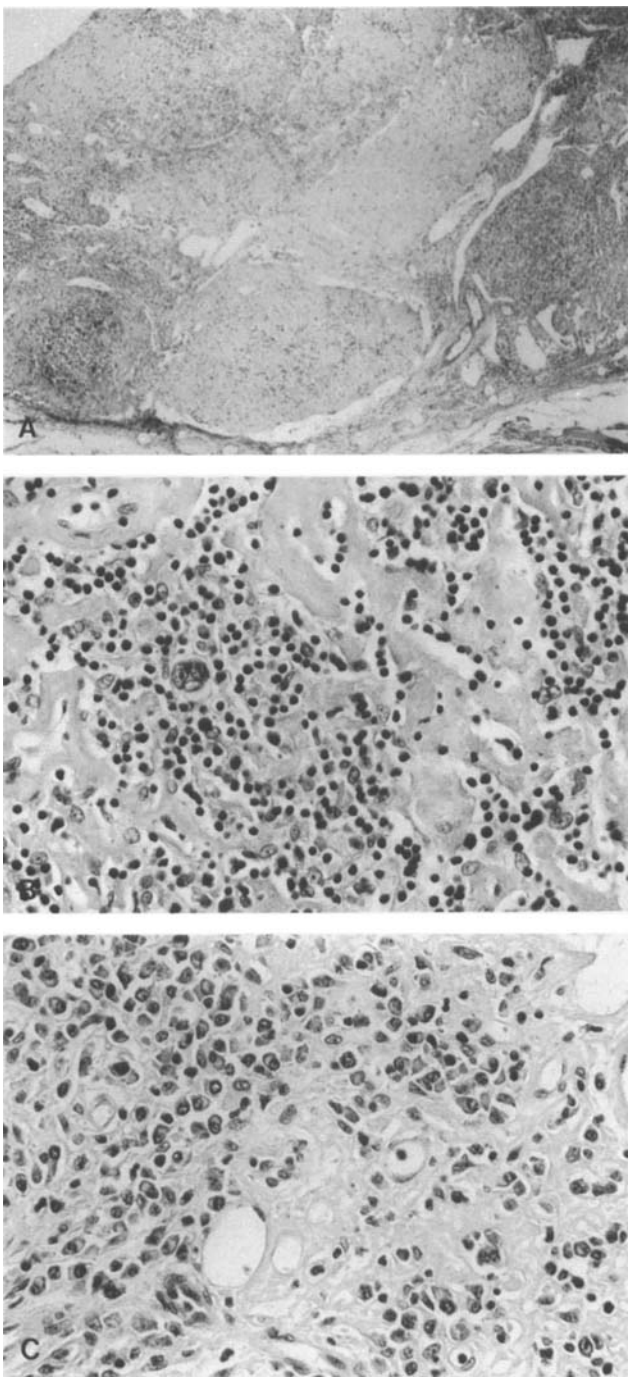

Fig. 1. Biopsy of a cervical node. A: Low-power view showing the nodular pattern associated with widespread sclerosis. B: Typical Reed-Sternberg cell among a few lymphocytes and fibrotic bands. C: Sheets of plasma cells among collagenous deposits.

probable, since medullogram and bone marrow biopsy were rich and displayed normal granulocytic differentiation. We did not perform a search for antineutrophil or antiplatelet antibodies, but the favourable response to plasmapheresis suggested the involvement of circulating autoantibodies, although we cannot exclude other soluble factors.

Auto antibodies could be directly produced by tumour cells, by nonspecific tumoral infiltrates, or being related to the immune regulatory phenomenon directed against HD. The absence of a monoclonal component in serum or urine, together with the absence of monotypic immunoglobulin detection in tumoral cells argue against the first hypothesis. Although its specificity was not determined in our patient, the antibody associated with AIHA in patients with HD has been identified as an anti transition (I^t) antigen antibody [6]. This antigen occurs during the transition from i to I antigen in the development of the erythrocyte Ii antigen system, that also exists on myeloid cells [7]. A modified Ii antigen expression or association on the surface of tumoral cells could lead to abnormal antibody synthesis. Finally, a dysregulated Ig production by normal cells infiltrating the tumour would be in line with the importance of the plasmacytoïd infiltrate observed in our patient and in at least two other cases [3,8].

We and others [9,10] have previously shown that R-SC are capable of modulating their environment by producing a number of cytokines, including interleukin-6 (IL-6), which could account for the polyclonal reactive plasma cell hyperplasia observed in our case. It is noteworthy indeed that histological analysis showed intermingled features of diffuse fibrosis (HD type 4) and nodular sclerosis (HD type 2), suggesting a sequential link between the two forms of the disease, an association not previously reported. Finally, the pathogenesis of HD cases with autoimmune manifestations could be related to a complex cascade of cytokine signals, in particular IL-6, orchestrated by R-SC, with the functional properties of these cells not elucidated.

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Thrombotic Thrombocytopenic Purpura and 17β-Estradiol Transdermal Skin Patch

To the Editor: Thrombotic thrombocytopenic purpura (TTP) is an uncommon disorder characterised by consumptive thrombocytopenia, microangio-

pathic hemolytic anemia, fever, bizarre neurological symptoms/signs, and renal involvement. The condition is associated with infections, systemic lupus erythematosus (SLE), pregnancy, estrogen therapy, neoplasms, and allogeneic bone marrow transplantation [1–4]. Two patients was diagnosed to have TTP in our department, and both gave a history of using the 17β-estradiol transdermal skin patch as a form of estrogen replacement therapy. As this form of estrogen replacement therapy has not been widely used in our community, its association with a higher risk of developing TTP, as compared to the more conventional oral estrogen therapy, is suspected.

The first patient was a 55-year-old woman had a history of SLE diagnosed 10 years ago. Both renal and cerebral involvement was reported at that time. She responded well to steroid therapy, and the SLE was quite inactive during the last few years. She had been using the 17β-estradiol transdermal skin patch (2 mg twice weekly, equivalent to an effective dose of 25 μg/day) for more than 5 years as estrogen replacement therapy after her menopause. She presented in September 1995 with easy skin bruising, tiredness, and passing dark-coloured urine for about 1 week. Physical examination revealed only the presence of generalised petechiae. The blood counts showed hemoglobin, 8.6 g/dl; white blood cell count (WBC), 6.6×10^9/L; platelet 17×10^9/L; and reticulocyte, 8%. Peripheral blood film revealed polychromasia and numerous schistocytes. Urinalysis showed mild proteinuria and the presence of hemoglobinuria. There was evidence of hemolysis: hyperbilirubinemia, absent serum haptoglobin, and raised methemalbumin.

Renal and liver function tests were otherwise normal. Serum lactate dehydrogenase (LDH) was six times elevated. The coagulation profile including prothrombin time (PT), activated partial thromboplastin time (APTT), thrombin time (TT), and fibrinogen level, were normal and the d-dimer was not raised. The Coombs test was negative and platelet-associated antibody not found. She still had a positive 1 in 360 antinuclear factor and a weakly positive anti-DNA. Serum C3/C4 levels were normal. Bone marrow biopsy revealed erythroid hyperplasia and increased megakaryocytes. A diagnosis of TTP was made. She responded promptly to repeated plasma exchange and fresh frozen plasma infusion with full normalisation of blood counts. Prednisolone 30 mg/day and enteric-coated aspirin 100 mg/day were also given.

The second patient was a 44-year-old woman. She was also using the 17β-estradiol transdermal skin patch (2 mg twice weekly, equivalent to an effective dose of 25 μg/day) for about 6 months, prescribed by her gynecologist for menorrhagia. She presented in July 1993 with fever, headache, and mental confusion. On physical examination, fever, jaundice, pallor, and generalised petechiae were noted. She was mentally confused, but there was no focal neurological sign. Blood counts showed hemoglobin, 7.2 g/dl; WBC count, 15×10^9/L; platelet count, 13×10^9/L; and reticulocytes, 17%. Peripheral blood film revealed polychromasia, numerous schistocytes and the presence of normoblasts. Urinalysis revealed hemoglobinuria. There were also evidences of hemolysis: hyperbilirubinemia, absent serum haptoglobin and raised methemalbumin. The liver function tests were otherwise normal. There were mildly raised serum urea (14.1 mmol/L) and creatinine (0.158 mmol/L). Serum LDH was 10 times elevated. The coagulation profile, including PT, APTT, TT, and fibrinogen level were normal and the d-dimer was not raised. Coombs test was negative and platelet associated antibody not found. Antinuclear factor and anti-DNA were both negative. Bone marrow biopsy revealed erythroid hyperplasia and increased megakaryocytes. A diagnosis of TTP was made. She responded repeated plasma exchange and fresh frozen plasma infusion. There was good neurological recovery, as well as complete normalisation of blood counts.

TTP has been recognized to have a strong association with estrogen therapy [4]. However, there is so far no evicence that any particular estrogen gives a higher risk. TTP is an uncommon disorder. As the major hematology referral centre in Hong Kong seeing hundreds of new cases a year, our department has had only three cases of TTP documented during the past $2\frac{1}{2}$ years, including the two patients described above. The third patient was a man with disseminated adenocarcinoma.

Because of its relatively high cost, the 17β-estradiol transdermal skin patch is not very commonly used in our community. Most of our patients requiring estrogen replacement therapy are using one of the oral preparations. Although the development of TTP in our two patients who were using the skin patch might be purely coincidental, we have the suspicion that the preparation may possibly be associated with a higher risk of the development of TTP. Further reports of similar cases will be useful in substantiating the hypothesis. The 17β-estradiol transdermal skin patch is often prescribed for physiological substitution and is used in postmenopausal women. Transdermal therapy with 17β-estradiol delivers the hormone in unchanged form directly through the skin directly into the bloodstream [5]. It raises the estradiol concentration to a level similar to that of the early to midfollicular phase, maintaining it over the application period. So far, there has been no report of associated coagulopathy or platelet abnormality with the preparation [5]. However, we are not certain as to whether this sustained constant level of estradiol provided by the transdermal system may render patients more susceptible to the development of TTP, especially in those with other risk factors, such as our first patient with SLE. Compared to the oral estrogen preparations, this appears to be a unique feature of the preparation. As TTP remains a rare disorder, further reports of similar cases will be required for confirmation.

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Acute Esophageal Stricture After Induction Chemotherapy for Acute Leukemia

To the Editor: Although dysphagia in patients with acute leukemia is usually related to reflux esophagitis, infectious esophagitis, chemotherapy [1], and leukemic infiltration [2], acute esophageal stricture resulting from chemotherapy in the patient with leukemia is very rare. I report here a patient with acute myelogenous leukemia who developed esophageal stricture within 1 month of chemotherapy.

A 40-year-old man was admitted with right middle lobe pneumonia in July 1995. A complete blood count showed hemoglobin of 8.4 g/dL, a white blood cell count of 4×10^9/L (62% blasts), and a platelet count of 84×10^9/L. The bone marrow examination revealed 5% myeloblasts, 86% promyelocytes, 1% proerythroblasts, 2% basophilic erythroblasts, 3% polychromatophilic erythroblasts, 1% orthochromic erythroblasts, and 2% lymphocytes. Some promyelocytes had multiple Auer rods and were myeloperoxidase positive. He was diagnosed as having acute myelogenous leukemia (AML) M3 and pneumonia. After the resolution of pneumonia, induction chemotherapy consisting of adriamycin (45 mg/m^2 D1-3) and