study of 24 paediatric patients with chronic ITP. In all, 15 patients had a complete response, 6 of whom relapsed at time points varying from 3 to 18 months. The other 9 patients still had ongoing complete responses (6 had responses lasting for ⩾1 year, 2 had continued responses at 24 and 30 months).[9] A case report of two patients with autoimmune thrombocytopenia and neutropenia who were treated with rituximab demonstrated sustained remission of thrombocytopenia in both patients, but only one patient had resolution of neutropenia.[10] There are two case reports of rituximab being used to treat ITP associated with CVID. In the first, rituximab resulted in only a partial response and a rise in platelet count to around 40×10^9/l.[11] The second patient had both ITP and neutropenia in association with CVID. After rituximab treatment, the platelet count rose to 130×10^9/l and the neutrophil count normalised. However, treatment was continued with steroids at a reduced dose of 10 mg/day.[12]

This case report describes the successful use of rituximab to treat ITP in a patient with CVID. The platelet count remains at $>150\times10^9$/litre 1 year after treatment, although the neutropenia has persisted, with neutrophil counts of around 0.8×10^9/litre. The anti-platelet autoantibodies have resolved, but granulocyte specific IgG is persisting. Why rituximab treatment led to the clearance of anti-platelet but not anti-granulocyte antibodies is not clear. Neutropenia has been associated with rituximab treatment,[13] but in this case our patient's neutropenia predated rituximab treatment by some years and antigranulocyte antibodies were present.

It is becoming increasingly apparent that rituximab has a place in the treatment of ITP, including when it is present in association with other conditions. The exact position of rituximab in treatment protocols is still to be determined, but for now it can probably be used when other treatment options have failed. Monoclonal antibodies are expensive, and, while rituximab is no exception, this has to be balanced against the cost of regular platelet transfusions, and the health and fiscal costs which result from the long-term use of steroids. A number of other questions remain, such as whether the full dose of 375 mg/m^2 used to treat B cell non-Hodgkin's lymphoma is also required for ITP, or whether a lower dose would still provide the same clinical benefit. The literature suggests that recurrence of ITP treated with rituximab should be expected, although after a variable time period lasting months to years. Whether re-treatment with rituximab at this stage is effective requires evaluation.

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doi: 10.1136/jcp.2006.041426

Accepted 17 November 2006

Competing interests: None declared.

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Two cases of cytokeratin positivity in atypical fibroxanthoma

Atypical fibroxanthoma (AFX) is a pleomorphic tumour, first described by Helwig in 1961.[1] AFX was thought to be a superficial form of malignant fibrous histiocytoma, but some describe AFX as a reactive lesion that can be confused with pleomorphic carcinomas. Clinically, AFX presents as a 1–2 cm rapidly growing, dome-shaped, polypoid nodule or plaque which may crust or ulcerate.[2] AFX is a low-grade sarcoma and is usually cured by excision; however, recurrence and rare metastases have been reported.[3]

Histological examination shows a dome-shaped nodule covered by a thin epidermis, which may be surrounded by a collarette of hyperplastic epithelium.[4] Tumour cells are spindle—or epithelioid—shaped, and may have foamy cytoplasm. Cells may be dispersed randomly or arranged in fascicles. Nuclei are large, pleomorphic, and may be hyperchromatic and multiple in number.

Immunohistochemistry is essential in the diagnosis of AFX, because many poorly differentiated cutaneous spindle-cell neoplasms have similar morphologies but stain differently. AFX is usually negative for S-100 protein, HMB45, desmin, CD34 and cytokeratin (CK).[5–7] Periodic acid Schiff stain fails to demonstrate glycogen in cells with foamy cytoplasm.[7] AFX is CD68 variably positive and procollagen positive. Rare staining for actin and CD1A has been reported.[6]

We report two cases of AFX that showed weak aberrant CK positivity. Two Caucasian men, each in his late 70s, presented with scaly, crusted nodules on the scalp and cheek, respectively. Excisional biopsies of both cases showed de-differentiated fibrohistiocytic neoplasms. Cells from both cases stained positive for procollagen-1 and CD68, negative for HMB45 and S-100 protein, and weakly expressed CK (figs 1 and 2). Based on these clinical and histological findings, a diagnosis of AFX was made in both cases.

Several theories have attempted to explain aberrant staining in cutaneous neoplasms. Tumour cells may inherently have epithelial antigens such as CK, or may take up epithelial

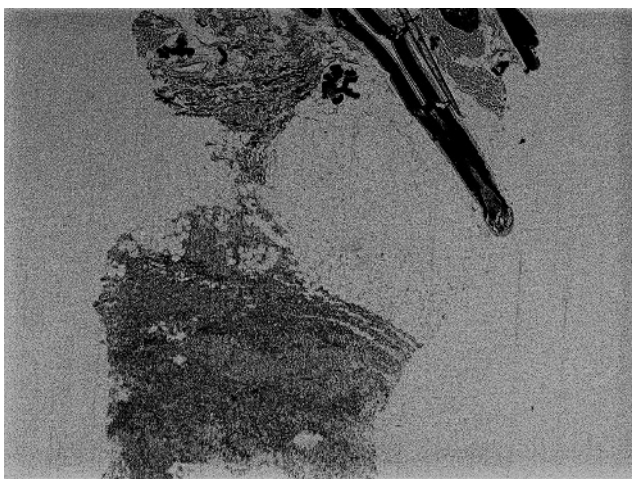

Figure 1 Atypical fibroxanthoma: case 1, cytokeratin. Note the diffuse, weak cytokeratin positivity in the deep dermis.

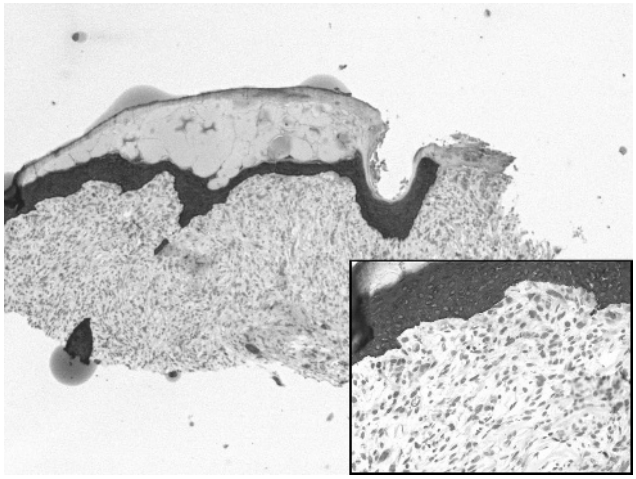

Figure 2 Atypical fibroxanthoma: case 2, cytokeratin stain. Note the faint dermal cytokeratin positivity.

antigens in their course of differentiation. Phagocytosis of CKs from other cells and adnexa is also a possibility. Conversely, these neoplasms may actually be de-differentiated squamous-cell carcinomas that have lost their epithelial antigens.

It is important to realise the inherent uncertainty in the diagnosis of poorly differentiated cutaneous malignant spindle-cell neoplasms. The most reliable way to distinguish these neoplasms is immunohistochemistry; however, dermatopathologists must keep in mind the capabilities and limitations of immunohistochemistry. Aberrant CK expression can occur in AFX. It is important not to overinterpret this aberrant staining, which might lead to an erroneous diagnosis.

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doi: 10.1136/jcp.2006.044206

Accepted 3 November 2006

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Pure red cell aplasia associated with type I autoimmune polyglandular syndrome—successful response to treatment with mycophenolate mofetil: case report and review of literature

Pure red cell aplasia (PRCA) is a rare haematological syndrome characterised by anaemia, reticulocytopenia and severe erythroid hypoplasia without alteration in megakaryocytic and myeloid maturation. Immune system irregularity can be mediated by the presence of autoantibodies against erythroid cells or against erythropoietin (Epo), or by hyperactivity of large granular lymphocytes with enhanced T cell or natural killer cell cytotoxicity.[1–3] The association between PRCA and other autoimmune diseases such as autoimmune polyglandular syndrome (APS) I is rare.[4]

The second autoimmune disease, named APS I or autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED), is a rare hereditary autosomal recessive disorder. It is characterised by the presence of chronic mucocutaneous candidiasis, multiple endocrinopathies (hypoparathyroidism, adrenocortical failure, hypergonadotropic hypogonadism, type I diabetes mellitus and panhypopituitarism), and various ectodermal manifestations (enamel dysplasia, nail dystrophy, alopecia, vitiligo and keratopathy).[5 6] Clinically, APECED can be confirmed by appearances of at least two of the three features: candidiasis, hypoparathyroidism and adrenocortical failure.[5–7] This is the first multiple autoimmune disorder shown to be caused by mutations of a single gene—the autoimmune regulator gene (AIRE).[8] This gene was mapped at 22q22.3 and consisted of 14 exons.[8] It is expressed in immune-related organs, such as thymus, lymph nodes and fetal liver, indicating that it has a pivotal role in the immune function. Its main role is to act as a transcriptional factor. Over 40 different mutations of the AIRE gene have been identified (point mutations, insertions and deletions).[8 9]

Case report

A 33-year-old woman was admitted to the Institute of Haematology, Belgrade, Serbia, in April 2001 for blood transfusion for the treatment of anaemia. The diagnosis of idiopathic hypoparathyroidism was made at age 7 years. At age 14 years, she developed idiopathic adrenal insufficiency and 2 years later, she developed mucocutaneous candidiasis. Since early infancy, she had had alopecia universalis. The patient had dysfunctional thyroid nodule, with positive anti-tireoglobuline and anti-microsomal antibodies. She had had euthyroid and amenorrhoea for the last 3 years. Her younger sister developed chronic mucocutaneous candidiasis, hypoparathyroidism, adrenal insufficiency, pernicious anaemia and lichen ruber planus. The DNA samples from the patient and her sister were additionally tested for a nonsense mutation in exon 6 (R257X) of the AIRE1 gene. PCR analysis and direct sequencing showed that both sisters were homozygotic for the R257X mutation. This change in arginine resulted in a truncated gene product. Physical examination revealed marked pallor, alopecia and oral candidiasis without lymphadenopathy or hepatosplenomegaly. MRI excluded the presence of thymoma. Laboratory findings revealed a haemoglobin level 60 g/l, red blood cells 1.4×10^{12}/l, haematocrit 13.7%, mean corpuscular volume 115 fl, reticulocytes 0.0%, platelets 395×10^{9}/l and white blood cells (WBCs) 11.7×10^{9}/l (segmented neutrophils 15% and lymphocytes 85%). Morphologically, lymphocyte populations dominantly consisted of small lymphocytes (43%), partly small T lymphocyte with irregular nucleus (22%) and larger activated lymphocytes (20%). The Coombs test was negative. The increased haemolysis and paroxysmal nocturnal haemoglobinuria were ruled out. The serum Epo level was markedly increased (47.3 mIU/ml) in comparison to reference values (9.9 (2.9) mIU/ml; range 7.0–12.8 mIU/ml). Further studies revealed normal values for serum ferritin, transferin, vitamin B_{12} and folic acid. Tests for antibodies against human parvovirus B19, cytomegalovirus, HIV, hepatitis B, C, and Epstein–Barr virus were negative. Antinuclear antibody, rheumatoid factor and anti-DNA antibody were not detectable. Bone marrow aspirate showed hypercellularity (>III), a lack of erythroid precursors (2% of bone marrow nucleated cells), normal granulocyte precursors (75%) and megakaryocytes, 16% of lymphocytes, 4% of plasmocytes and 3% of monocytes. Bone marrow biopsy revealed slight hypercellularity with normal maturation of the myeloid lineage and megakaryocytes, but <1% of the cells were erythroid precursors (including proerythroblasts). There was no increase in the blast count. The karyotype was normal. Immunophenotyping (Flow cytometry, Becton Dickinson, San Jose, USA) performed on peripheral blood cells showed that 91% (8.21×10^{9}/l) of all cells were mature T lymphocytes (CD2, CD3, CD5, CD7, CD4 or CD8, T cell receptor (TCR)α/β or TCRγ/δ)+. T cell subsets expressed 62.98% (5.15×10^{9}/l) of the TCR α/β+ T cells and 28.69% (3.06×10^{9}/l) of TCRγ/δ+ cells. A small subset, 9% (0.89×10^{9}/l), of mature phenotype B lymphocytes (CD19, CD20, CD24, SIg, κ or