

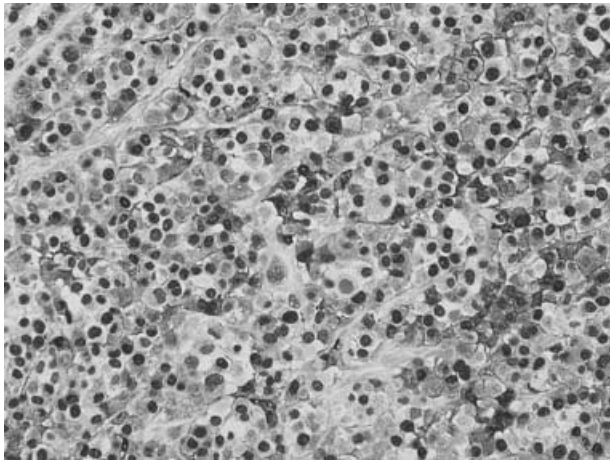


fig. 2 Intense immunohistochemical staining with S-100 protein.

excision. A subsequent total body positron emission tomography (PET) scan did not show hypermetabolic hot spots. After 13 months, a rapidly growing nodule in the left axilla revealed, after resection, a subcutaneous lymph node metastasis. The patient is currently followed by the Oncology Department for systemic chemotherapy.

Sentinel lymph node biopsy represents a dramatic advancement in the management of melanoma and breast cancer, since it allows a reliable nodal pathological staging without the morbidity of elective radical lymphadenectomy. The potential for SLB in the management of high-grade sarcomas like CCS is at present unclear.⁴ Picciotto *et al.* and Nishida *et al.* reported the presence of positive SLN in two cases of CCS.^{5,6} Al-Refaie *et al.* detected metastatic SLNs in one out of three CCS (three positive nodes out of three SLNs, plus a positive node found at the subsequent lymphadenectomy). This patient developed early bony metastases, suggesting concurrent nodal and distant metastases from an advanced tumour.⁷ Van Akkooi *et al.* reported positive SLNs in two out of five patients, with additional metastatic nodes found after lymphadenectomy.⁸ Recurrent disease was observed only in these two patients. The authors conclude that SLN status seems predictive of additional node involvement and recurrence. The limited reported observations do not allow to draw reliable conclusions. Our case showed distant subcutaneous metastases in the absence of positive SLN, indicating an early haematogenous invasion. The SLN negativity makes the blood origin likely also for the axillary lymph node metastases. Also in the previously reported cases of disseminated disease,^{7,8} no evidence of sequential tumour progression is apparent; thus, the SLN positivity may simply reflect an advanced disease with parallel nodal and visceral involvement. The usefulness of the SLB technique is based on the assumption of a consistent 'orderly progression'

of metastases, i.e. regional lymph node should be invaded in a sequential manner before distant spreading. In case of random nodal metastatic pattern or concurrent lymphatic and haematogenous invasion, SLB becomes unreliable as a prognostic tool. Further observation are needed to correctly assess the value of SLB in the management of CCS.

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Two cases of atopic dermatitis-like conditions induced in psoriasis patients treated with infliximab

Editor

Psoriasis is usually described as a Th1-dominated disease [e.g. lymphocytes in the skin produce interleukin 2 (IL-2)]

and interferon-gamma (IFN- γ)]¹. Tumour necrosis factor- α (TNF- α) is a key inflammatory cytokine in inflammatory diseases and is expressed by keratinocytes, Langerhans cells and T lymphocytes in psoriasis.²

Blocking either TNF- α or TNF- α receptors with antibodies is a therapeutic option in the treatment of psoriasis. Infliximab is a humanized murine monoclonal IgG1 antibody that blocks the binding of TNF- α to its receptor. Furthermore, it binds transmembranal TNF- α and mediates killing of TNF- α -positive cells.²

Atopic dermatitis (AD) is, in the acute phase, a Th2-dominated disease (lymphocytes in the skin produce IL-4, -5 and -10) but in the chronic phase, a mixed Th1/Th2 disease. TNF- α is produced by the mast cells.³

Down-regulation of Th1 cytokines may result in an overexpression of Th2 cytokines leading to manifest Th2-dominated diseases. AD-like conditions have been reported after infliximab therapy of rheumatoid arthritis, psoriasis arthritis and Crohn's disease.⁴⁻⁶

A 46-year-old Caucasian man with severe suberythrodermic psoriasis vulgaris and psoriatic arthritis and a family history of psoriasis as well as a history of atopy and hand eczema, had received ultraviolet B phototherapy, coal tar, and topical steroids with insufficient effect. Systemic methotrexate resulted in increased blood liver enzymes.

Cyclosporin (3 mg/kg per day) was insufficient; therefore, infliximab (5 mg/kg) was added at weeks 0, 2, 6 and 14, followed by infusions every 8th week.

After three infusions, the psoriasis and psoriasis arthritis had improved. After the seventh infusion the patient developed severe impetigo and was treated with dicloxacillin (500 mg three times a day for 10 days), while infliximab was paused.

Two days after the following infliximab infusion the patient was admitted with severe erythroderma and eczematous eruptions on the trunk, the back, the arms, and the face; impetigo; and a positive blood culture for *Staphylococcus aureus*. The patient was treated with dicloxacillin, as described above, and topical steroids, and the cyclosporin treatment was increased to 200 mg daily. Biopsies showed AD, which was supported by a total serum IgE of 16 163 (normal < 150). After stopping infliximab the eczema disappeared and psoriasis reappeared.

A 68-year-old Caucasian man with severe pustular and plaque-type psoriasis (fig. 1a) treated with acitretin, mycophenolate mofetil, hydroxyurea, sulfasalazine and alefacept without effect, commenced infliximab therapy. The patient had recurrent rhinitis.

Infliximab infusions resulted in marked improvement. At the 8th infusion the patient developed eczema spreading from the shin to the trunk, the back and the upper extremities especially in the elbows and the dorsal side

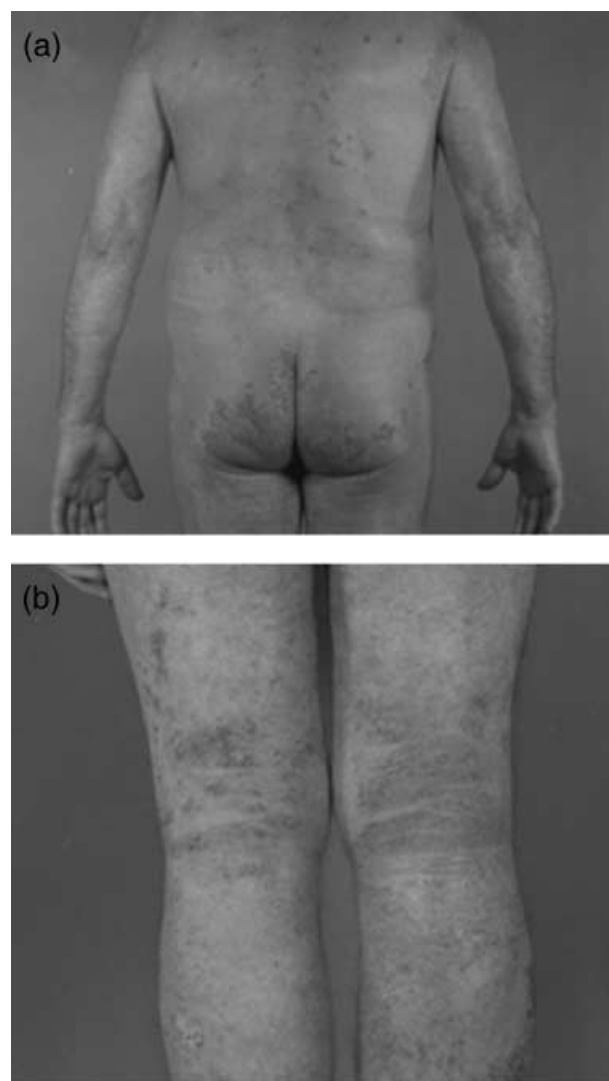


fig. 1 (a) Patient from case 2, before treatment with infliximab. (b) The same patient after treatment with eight infliximab infusions.

of the knees (fig. 1b). He had impetigo, eosinophilia and increased C-reactive protein. A biopsy showed histology consistent with dermatitis. Infliximab therapy was stopped and the patient was treated with topical steroids and dicloxacillin 500 mg three times a day for 10 days. Cyclosporin treatment (3 mg/kg per day) was initiated and the eczema disappeared within few weeks. Upon decrease of the cyclosporin dose the psoriasis recurred.

Atopic dermatitis was previously described in infliximab-treated patients suffering from Th1-dominated diseases⁴⁻⁶ who all had a history of atopic diseases. However, TNF- α is not a Th1 cytokine *per se* as IL-2 and IFN- γ ,⁷ and blocking TNF- α 's action should not necessarily lead to a Th2-dominated disease. Thus, in a study of nine

AD patients treated with infliximab, the patients initially improved, but improvement could only be maintained in two of the patients.⁸ Although the mechanisms underlying the anti-TNF- α -therapy-induced AD-like eczema remains unknown, patients with a history of atopy should be monitored closely during anti-TNF- α therapy.

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An unusual complication of systemic lupus erythematosus: bacterial meningitis caused by *Streptococcus agalactiae*

Editor

Patients with systemic lupus erythematosus (SLE) are prone to certain infections and such infections maybe a common cause of morbidity and mortality. Intrinsic

immunological defects, immunosuppressive and cytotoxic medications are implicated to be an important attributing factors which influence infections in SLE.^{1,2} However, central nervous system (CNS) infection in patient with SLE is rare, constituting only up to 3% of all infections.³ CNS infections is most often caused by *Cryptococcus*.³ As to our knowledge, bacterial meningitis due to *Streptococcus agalactiae* in SLE has not been reported previously.⁴

An 18-year-old Korean girl who had recently been diagnosed of SLE was admitted to our emergency room with high grade fever, vomiting and severe headache for 5 days. The characteristic of her headache was dull without specific localization or associated symptoms. Her SLE had been diagnosed at our clinic 2 weeks ago with initial presentation of ill-defined erythematous and purpuric reticular patches on her face and extremities, and 3-month history of polyarthritis and deep-vein thrombosis. Antinuclear antibodies, high titres of antibodies to double-stranded DNA, and low C3 and C4 level were detected, whereas antiphospholipid antibody and anticardiolipin antibody were negative. She had been taking systemic corticosteroids (methylprednisolone 16 mg/day) for 1 week on her visit to emergency room.

Upon admission, physical examination showed stuporous mentality, neck stiffness, body temperature of 39 °C without any focal neurological signs. Laboratory evaluation revealed suspicious findings of infection such as neutrophilic pleocytosis, increased C-reactive protein. Cerebrospinal fluid (CSF) analysis revealed elevated opening pressure, increased white blood cells, elevated protein level and depressed glucose level. India ink staining was negative for cryptococcal capsule. But, on CSF culture, *Streptococcus agalactiae* was identified by VITEK® 2 (bioMérieux, Marcy l'Etoile, France). She was given antibiotics (ceftriaxone 4 g/day) intravenously and corticosteroid (prednisolone, 50 mg/day) orally. After 1 month of treatment, full recovery of CNS symptoms with no neurological sequelae were observed.

Streptococcus agalactiae is known to be a major cause of sepsis and meningitis in human neonates and a frequent origin of peripartum fever in adults.⁵ But it had not yet been reported as an infection focus of meningitis in SLE patients since it usually does not cause opportunistic infections.

It is difficult for patients and physicians to recognize the early signs and symptoms of CNS infections as the manifestation of the infection process may mimic CNS features of SLE.⁶ Therefore, we think that physicians should be constantly aware of CNS infection in SLE. If symptoms of CNS infection and signs of elevated C-reactive protein are present, CSF analysis should be quickly performed and appropriate management is required to reduce mortality.