polyclonal EBV infection and suggested a non-malignant lesion. As further reduction of immunosuppressive therapy was required, tacrolimus was gradually discontinued. EGDs performed 2 months later showed healing ulcers and a marked decline in EBV (10 copies/μg DNA). Tapering the immunosuppressant did not cause sJIA relapse.

Though EBV-associated post-transplant lymphoproliferative disease can affect the GI tract [1], there are few reports of EBV-related GI disease in immunosuppressed patients with rheumatic disease [2, 3] and no reports of paediatric cases. Diagnostic criteria for GI inflammation caused by EBV have not been established, therefore diagnosis in reported cases was based mainly on EBER-1+ lymphocyte infiltration of the lesions [4–8]. Several recent studies indicate that q-PCR of biopsy specimens is helpful for diagnosing CMV-associated colitis [9] and EBV-associated chronic atrophic gastritis [10]. Indeed, q-PCR supported the diagnosis in our case. Although both EBV and CMV DNA were isolated from the GI lesions and gradual withdrawal of tacrolimus eradicated the viruses and reduced GI inflammation, it was not until EBV was eliminated from the mucosa that the gastric ulcer healed (despite early elimination of CMV). The clinical course indicated that the main cause of GI inflammation was EBV rather than CMV, which was also locally reactivated.

This case shows that EBV infection should be considered when GI inflammation is observed during immunosuppressive therapy for rheumatic diseases. Immunohistochemistry and site-specific detection of viral genome are useful for the diagnosis of GI lesions caused by EBV.

**Rheumatology key message**

- EBV infection should be considered in immunosuppressed patients with rheumatic disease and GI inflammation.

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Rothmund-Thomson syndrome—a single case report with systemic muscular atrophy, multiple organ fibrosis and pulmonary cachexia

Sir, Rothmund-Thomson syndrome (RTS), also called poikiloderm congenitale, is a rare autosomal recessive inherited disorder characterized by a generalized rash, which first appears in infancy, and skeletal abnormalities and malignancies [1]. However, little is known about the overall longevity of RTS patients and how they age in the absence of malignancy because clinical follow-up data are very limited [2].
We report here a woman with RTS who died at the age of 42 years after multiple organ failure, including chronic end-stage renal disease (ESRD), exocrine pancreatic insufficiency, lung fibrosis and lethal respiratory insufficiency due to progressive systemic muscular atrophy. The patient was first admitted to Hannover Medical School with febrile infection due to relapsing chronic sinusitis as well as palpitations and muscular weakness at the age of 24 years. No hereditary diseases were known in the larger family. Since her first year of life, skin atrophy on the cheeks, telangiectases on arms and legs and clinodactyly as well as alopecia totalis had been present (Fig. 1). On that first admission, the patient was able to walk only short distances and had difficulty with steps due to both-sided contractures in the Achilles tendons with equine foot deformities. Stature was short and body weight was rather slim (53 kg, 1.66 m, BMI 19.2 kg/m$^2$). Hyperopia required strong glasses for correction and defective dentition was documented, but there was no evidence of cataracts or other skeletal anomalies. Further testing revealed signs of Wolff-Parkinson-White syndrome, renal insufficiency with light proteinuria and haematuria as well as secondary hyperparathyroidism, IgG4 deficiency and myopathy. The final diagnosis of RTS was made on clinical grounds in 1985 by the department of dermatology and ascertained by means of skin biopsy. In the clinical course, reduced muscular mass in the shoulder girdle and creeping progressive muscular weakness in both arms increased, which was resistant to intermittent cortisone treatment. Climbing stairs became even more difficult because of general muscular atrophy and tenderness of the upper and lower limbs, and the progressive musculoskeletal syndrome led to more severe ventilatory insufficiency, diminished mimic and dysphagia. An enchondroma in the right tibia was operatively excised. An abdominal CT scan excluded malignancies but revealed shrunken kidneys, fatty pancreas degeneration with pseudocysts, fatty inclusions in autochthonic back muscles, skeletal dysplasia, osteopenia and interstitial opacities in both-sided basal pulmonary segments. Intermittent substitution of levothyroxine and pancreatic enzyme replacement therapy was performed because of, respectively, latent hypothyroidism and exocrine pancreatic insufficiency. BMI slowly decreased to 15.2 kg/m$^2$ (42 kg, 1.66 m) and the patient developed terminal ESRD so that chronic haemodialysis was begun at the age of 40. Later a percutaneous gastroenterostomy was established. Recurrent pulmonary infections then occurred and led to several hospital admissions with increasingly reduced general condition and progressive pulmonary cachexia (Fig. 1). On her last admission at the age of 42, the patient presented with a septic community-acquired pneumonia due to generalized muscular atrophy and pulmonary cachexia (30.8 kg, 1.66 m, BMI 11.2 kg/m$^2$). Although i.v. antibiotic therapy was started immediately, the respiratory situation became progressively worse and the patient died peacefully in the arms of her family.

The clinical findings of RTS have generally been provided through reports of single or small series of patients, leading to a total of 260 patients reported in the world literature so far [1, 2]. To our knowledge, our patient is one of the oldest described in the current literature. Revised guidelines for the diagnosis and management of RTS were determined in a multinational collaborative study.

**Fig. 1** RTS includes alopecia, generalized rash as well as pulmonary cachexia and generalized myopathy.

These photographs show the generalized rash with erythematous and macular changes and interspersed areas of dermal atrophy as well as alopecia in infancy (left) and adolescence (centre). The picture on the right outlines pulmonary cachexia with respiratory global insufficiency and generalized myopathy as an adult of 42 years some months before death.
from Wang et al. [2]. The clinical history of our patient was characterized by progressive systemic muscular atrophy, which had previously been mentioned in two other case reports of younger patients with RTS [3, 4]. The long-term course of the progressive musculoskeletal syndrome resulted in severe cachexia and generalized fibrosis with progressive organ failure of kidneys, pancreas and lungs. Interestingly, a recent report from members of two generations of a South African family of Caucasian genetic background suggested an autosomal-dominant syndrome comprising poikiloderma, tendon contractures and progressive pulmonary fibrosis [5]. This entity differs from other poikiloderms and represents a unique syndrome of hereditary sclerosing poikiloderma, which has not been documented previously [1]. In comparison with the latter, our patient primarily suffered from muscular atrophy leading to pulmonary insufficiency while lung fibrosis developed at a later stage of the disease. Our patient also demonstrated extensive fatty infiltration of the pancreas and peripheral skeletal muscle as previously documented in one member of the South African family with extensive fatty infiltration of the pancreas. In summary, our data demonstrate that progressive pulmonary fibrosis may also occur in hereditary sclerosing poikiloderma of the RTS variant, and may be lethal in adulthood even with meticulous medical care.

Rheumatology key message

- This case highlights the importance of a musculoskeletal syndrome in the long-term course of RTS.

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Comment on: Non-infectious pulmonary toxicity of rituximab: a systematic review

Sir, Although there is at least one other systematic review to suggest the pulmonary toxicity of rituximab (RTX), there is a need to clarify that the majority of RTX-associated interstitial lung disease (RTX-ILD) reported was in non-rheumatological disorders (RDs).

From the study published in Rheumatology [1], out of 121 cases of potential RTX-ILD reported, the majority of RTX was prescribed for non-RDs (95%) and only six cases (three for rheumatoid arthritis and three for SLE) were due to RDs.

The mean dosage of RTX administered in hematological disorders was 4500 mg/m², and the calculated dose for an average adult (1.73 m²) was 7785 mg. The average RTX dose administered in RDs was 2000 mg, which is nearly four times lower than that for hematological disorders. Also, the average cumulative dose of RTX before the onset of symptoms of ILD was 1500 mg/m² or 2595 mg per adult, which is more than the average RTX dose for RDs. The mean number of RTX cycles before disease manifestation was 4.1, and in RDs, typically, RTX is given in two cycles (0 and 15 days).

Phase III trials recorded in post-marketing surveillance have shown that RTX-ILD is of less severity in RDs than in lymphoma. It is also reported that the overall RTX-induced lung injury is <0.03% of cases [2, 3].

A similar systematic review identified 45 cases of RTX-induced lung disorder. However, among them there was only one case where RTX was prescribed for an RD. On lung biopsy, this case was proved to be organizing pneumonia as opposed to ILD [4]. Soubrier et al. [5] reported two other cases of RTX-induced lung disease that turned out to be organizing pneumonia on biopsy, which improved with steroid therapy, ensuring a full recovery [5].

Another study that looked into the safety of RTX in RA patients with pre-existing lung disease did not show any new safety concerns other than what could be expected in long-standing RA with concomitant lung disease [6].

Although no controlled clinical trials have reported that RTX benefits the treatment of refractory ILD associated with scleroderma and antisynthetase syndrome, there are case reports where patients have benefited clinically and improved radiologically after RTX treatment [7, 8].

We conclude that although there are reports of RTX-associated lung disease, readers should be aware that the majority of the cases were in non-rheumatological disease, where the RTX dosage used is much higher than for RDs. Also on lung biopsy, the majority of these cases in RA patients were found to be organizing pneumonia, which responds much better to treatment with corticosteroids than ILD. High-resolution CT scan is a sensitive screening tool to differentiate the various forms of lung disease, such as organizing pneumonia and ILD, and