Eosinophilic fasciitis (EF) is a rare fibrosing disorder of the fascia of unclear aetiology and pathogenesis (1). First described in 1975, Shulman (2) reported EF as a connective tissue disorder characterized by a symmetrical painful swelling with progressive induration of the skin and soft tissues. There are no international diagnostic criteria for EF; diagnosis is based on clinical characteristic abnormalities and pathological features of a thickened fascia with an inflammatory infiltration.

EF has been reported in association with factors such as strenuous physical activity (2), *B. burgdorferi* infection (3), radiotherapy (4), malignancies, autoimmune disorders, and allogeneic bone marrow transplantation (AlloBMT) (5). It is difficult to diagnose EF, especially in patients undergoing AlloBMT, because chronic graft-versus-host disease (cGVHD) resemble EF in appearance (5). We report here a patient who received AlloBMT and developed EF 2 years later, and discuss how to distinguish EF from cGVHD.

CASE REPORT

A 51-year-old man, who had been diagnosed with acute myeloid leukaemia 3 years previously, underwent AlloBMT 2 years previously and was given cyclosporine and prednisolone for cGVHD prophylaxis. All immunosuppressive medications were gradually tapered and discontinued because no cGVHD was found. The course of immunosuppressive treatment was approximately 2 years. However, since the withdrawal of immunosuppressive medication, the skin over the patient’s bilateral arms and upper trunk showed diffuse erythema and swelled progressively, with no changes over the mucosa, face, scalp, and digits. Initially, cGVHD was suspected. Localized scleroderma and other scleroderma-like disorders were also taken into consideration. A complete blood count showed haemoglobin 13.7 g/dl, white blood cells 11.4×10^3/µl (neutrophils 61%, lymphocytes 23%, monocytes 5%, eosinophils 10%, myelocytes 1%, and no atypical cells) and platelet count 187×10^3/µl. Laboratory studies showed normal levels of glutamic-oxaloacetic transaminase (GOT) (25 U/l; normal <40), glutamic-pyruvic transaminase (GPT) (32 U/l; normal <63–93) of patients with EF during the acute phase. Elevated ESR and polyclonal hypergammaglobulinaemia were observed in 29% and 35%, whereas the subcutis and fascia in cGVHD are usually unremarkable (9–11) (Table SI). Moreover, eosinophilia (8.6%) was found together with the onset of appearance of skin change. Since then, eosinophilia persisted for one month, and then decreased to normal (1.8%) later. His skin evolved to a ‘‘peau d’orange’’ appearance (Fig. 1a, b). A skin biopsy was obtained 4 months after the initial change in the appearance of the skin. Histopathologically, the epidermis was unremarkable. The adnexal structures were preserved with mild dermal fibrosis. The fascia thickened and showed infiltration of plasma cells, lymphocytes and a few eosinophils (Fig. 1d, e). Magnetic resonance imaging scans revealed diffuse thickening and hyperintensity in superficial and deep muscle fascia that confirmed fascia inflammation (Fig. 1d, e). Finally, eosinophilic fasciitis was diagnosed. Treatment with oral prednisolone, starting at 30 mg daily, resulted in a rapid decrease in ESR, from 64 to 17 mm/h, and a progressive improvement in clinical appearance.

DISCUSSION

In general, the scleroderma-like appearance in patients who undergo AlloBMT is mostly reminiscent of the diagnosis of cGVHD. However, our patient was more likely to have EF. While the initial oedematous phase may be indistinguishable from early sclerodermatous skin changes, the irregular, woody, peau d’orange texture of EF is distinct from the morphea-like plaques or large confluent sclerotic areas with atrophic and shiny surface seen in patients with sclerotic GVHD. Lack of internal organ involvement, and sparing of the head and mucosa area, are characteristics of EF (6–8). In contrast, all skin and mucosa may be invaded in sclerodermoid GVHD, and diarrhoea, liver dysfunction and systemic disorder can occur frequently (9–11) (Table SI). Histopathologically, in EF the epidermis is usually intact with mild dermal fibrosis. Subcutis and fascia thickening associated with inflammatory cells infiltration, comprising lymphocytes, plasma cells, histiocytes, and eosinophils in variable degrees, are the hallmarks of EF (6–8). By contrast, sclerodermoid GVHD is characterized by atrophic epidermis, and the dermis is thickened with sclerotic change and destroyed adnexal structures, whereas the subcutis and fascia in cGVHD are usually unremarkable (9–11) (Table SI). Moreover, eosinophilia in the fascia in EF distinguishes it from GVHD.

Peripheral eosinophilia is a common feature among 63–93% (12) of patients with EF during the acute phase of the disease. Elevated ESR and polyclonal hypergammaglobulinaemia were observed in 29% and 35%,
respectively, in a case series (5). Antinuclear antibody and rheumatoid factor are almost always negative. Liver enzymes (GOT, GPT, ALP, γGT, total bilirubin) are usually elevated in cGVHD, but not in EF, which can aid in differentiating between the 2 disease entities (Table SI1).

Some authors consider that EF is a deep variant of cGVHD (13–15); however, a few case reports have shown other aetiologies, such as an association with Borrelia infection (3) and local irradiation (4) that do not have a history of AlloBMT. To our knowledge, eosinophilia in tissue or blood is important evidence in EF, but it is seen less frequently in cGVHD where donor-derived, alloreactive CD4+ and CD8+ T lymphocytes play key roles. However, in the rare circumstances of overproduction of IL-5, patients with cGVHD may have peripheral eosinophilia and will manifest as EF (13). Although EF has unique pathogenesis and a different presentation in terms of clinical, histopathological, and laboratory findings, it may be considered as a subtype of cGVHD (13–15).

We conclude that patients with features of EF should be offered a full-thickness biopsy, comprised of skin, muscle and fascia, and an extensive blood examination. In addition, MRI may be a helpful tool, as it can detect the pattern of the involved area, as diffuse or focal, and to monitor the response to therapy.

The authors declare no conflicts of interest.

REFERENCES