Lymphoedema manifesting with sudden onset of swelling of one whole leg suggests proximal obstruction of lymphatic drainage. In the developed world, lymphoedema due to venous or lymphatic obstruction in the pelvic area commonly results from damage or removal of regional lymph nodes through surgery or radiotherapy. By contrast, the most common cause worldwide is filariasis (the direct infestation of lymph nodes by the parasite *Wuchereria bancrofti*). Cancer rarely presents with lymphoedema except in advanced examples that present late, such as prostate cancer, in which venous obstruction might coexist. We report a rare case of extranodal marginal-zone B-cell lymphoma of the dura mater, which relapsed 28 years later in the form of a massive unilateral lymphoedema of the left leg.

A 52-year-old man complained of an enormous reduction in mobility caused by increasing swelling of the left leg over 4 weeks. 28 years previously (1971), a reticulosarcoma of the dura mater was diagnosed and the cerebral tumour had a complete resection and radiation. During the following 11 years no new disease was detected, but 17 years later a relapse in left parailiac lymph nodes was noted. On physical examination, the patient had a girth of the left thigh (79 cm) and of the left lower leg (52 cm), compared with the right side (29 cm and 24 cm, respectively; figure 1A). There was tender oedema of the whole leg, including the feet and ankles, with multiple skin-coloured papules showing lymphostasis-related papillomatosis cutis (figure 1B).

Laboratory investigations showed healthy blood-cell counts, healthy peripheral blood smears, a raised erythrocyte sedimentation rate of 45 mm/h, an elevated C-reactive protein concentration of 37 mg/L (healthy, <6 mg/L), a lactate dehydrogenase value of 284 IU/L (healthy, <248 IU/L), and a blood-urea nitrogen value of 457 μmol/L (healthy, <417 μmol/L). A CT scan showed a bulky tumour of 12×8×5 cm on the left parailiac region with compression of the iliac blood vessels (figure 1C). Enlarged hilar and axillary lymph nodes were also noted. Colour-encoded doppler sonography of the left leg excluded deep-vein thrombosis. Histological examination of a parailiac lymph-node biopsy sample showed an atypical lymphocytic infiltrate with absent lymph node architecture. The infiltrating cells were mostly made up of small, atypical lymphocytes with a centrocyte-like morphology, mixed with plasma cells and occasional blasts (figures 2A and 2B). The centrocyte-like cells were located in the expanded marginal zone, but also showed follicular colonisation. Immunohistochemically, the atypical cells expressed CD20 (figure 2A), CD79A, BCL2 and surface IgM, but were negative for CD5, CD10, cyclin D1, BCL6 and CD23. A marginal-
zone B-cell lymphoma was diagnosed. Notably, the histopathological reassessment of the so-called reticulosarcoma 28 years ago showed morphological features and an immunological profile identical to the lymph-node manifestation (figures 2C–F). Therefore, the diagnosis of reticulosarcoma was corrected to primary extranodal marginal-zone B-cell lymphoma of the dura mater.

To formally prove identity of both tumour-cell populations (primary dural and nodal lymphomas), PCR was done to amplify the clonal immunoglobulin heavy chain (IgH) gene rearrangements. Unfortunately, the DNA extracted from the 28-year old biopsy sample was completely degraded, preventing the generation of IgH-specific PCR products. The successful amplification and sequencing of the clonal IgH PCR products from the lymph node (figure 2B) showed a VH3 rearrangement with 15 somatic mutations, indicative of postgerminal centre tumour-cell derivation.

Figure 2: Cell histology
(A) Positivity of the nodal cells for the B-cell antigen MS4A1 (alkaline phosphatase-anti-alkaline phosphatase complex, original magnification ×100). (B) GeneScan analysis after IgH-PCR of the lymph-node biopsy. A monoclonal peak of 275 bp was identified. Red=size standard. Blue=fluorescence-labeled PCR products. (C) Dense infiltration of atypical lymphocytes in the area neighbouring the dura mater (Giemsa, original magnification ×100). (D) Increased magnification of the cerebral lymphoid infiltrate consisting of monocytoïd and centrocyte-like cells; (Giemsa, ×400 original magnification). (E) Positivity of the cells for MS4A1 (×400 original magnification). (F) Monotypic expression of the tumour cells for IgM (peroxidase antiperoxidase method, original magnification ×400).
The patient, diagnosed with relapsed extranodal marginal-zone B-cell lymphoma of the dura mater (stage IIIA), received six cycles of mitoxantrone, chlorambucil, and prednisone chemotherapy. This treatment resulted in complete remission with regression of the lymphoedema after three cycles. Unfortunately, the patient died 6 months later because of cardiac failure.

Extranodal marginal-zone lymphoma is a low-grade B-cell lymphoma which arises in several sites, most commonly in the stomach. It is associated with infections (eg, *Helicobacter pylori*) and autoimmune disease (eg, Sjögren’s syndrome of the salivary glands). Irrespective of the location of origin, these types of tumour have much of the same clinical, pathological, and molecular features. They usually show a slow progression, often remaining localised to their sites of origin for many years before dissemination.

Primary CNS lymphomas are a rare form of extranodal non-Hodgkin’s lymphoma that account for 4% of all primary cerebral tumours. Most primary CNS lymphomas are high-grade B-cell lymphomas of the diffuse, large B-cell lymphoma type. The outlook for these patients is poor, with median survival time ranging from 30 to 60 months with combined radiation and chemotherapy. Primary extranodal marginal-zone B-cell lymphomas of the dura mater, by contrast, are exceedingly rare. Since the first description of a dural low-grade B-cell lymphoma of mucosa-associated lymphoid tissue type by Kumar and colleagues, only a further eight examples have been reported. Similar to their counterparts in other locations, extranodal marginal-zone B-cell lymphomas of the dura mater are usually slow to progress. Notably, by contrast with classical high-grade primary CNS lymphomas, remission or cure could be achieved by local treatment modalities in most individuals with extranodal marginal-zone B-cell lymphomas of the dura mater. Nearly all examples remained localised to the primary site, and long-standing, complete remission was achieved after total excision, local radiation, or chemotherapy after a follow-up of between 3 and 63 months. The patient with a follow-up of 28 years gives the unique opportunity to study the long-term outcome of a patient with this type of tumour. By contrast with the previous examples, this patient developed two recurrences: the first (cervical lymph node) 11 years after the initial diagnosis of extranodal marginal-zone B-cell lymphomas of the dura mater, and the second (widespread nodal involvement) a subsequent 17 years later. Both recurrences were treated successfully. High-grade transformation of the lymphoma cells, as described in some extranodal marginal-zone B-cell lymphomas in other locations, was not seen in our example, or in any of the previously-reported tumours of this type.

In conclusion, extranodal marginal zone B-cell lymphomas of the dura mater are slow developing and usually localised. This entity should be recognised by clinicians and pathologists, and distinguished from the more aggressive primary, cerebral, large B-cell lymphomas, which are associated with a much poorer outcome.

Acknowledgments
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Conflict of interest
We declare no conflicts of interest.

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