P617

Twenty-first Meeting of the European Neurological Society – Lisbon, 28 – 31 May 2011

Radiation-induced malignant peripheral nerve sheath tumors – a report of 2 cases.

Rémy Phan-Ba[1, 2], MD, Shibeshih Belachew[1, 2], MD PhD, Zayd Jedidi[2], MD, Brieuc Sautois[3], MD, Manuel Deprez[4], MD PhD, Gustave Moonen[2], MD PhD

[1]MYelin Disorders ReseArch teaM (MYDREAM), Liège, Belgium; [2]Department of Neurology, C.H.U. of Liège, Liège, Belgium; [3]Department of Haematology, C.H.U. of Liège, Liège, Belgium; [4]Department of Pathology, C.H.U. of Liège, Liège, Belgium

Case n°1 :

A sixty year-old woman was seen for a 2 year history of right cervical and arm neuropathic pain, associated with an arm weakness. She mentionned a loss of 5 kilograms over the past year. The neurological examination depicted a severe weakness, atrophy and loss of sensation in from the right C4 to C7 radicular territories, predominating in C5-6 with decrease of all deep tendon reflexes in the right arm without signs of central nervous system involvement. A subclavicular hardened and enlarged lymph node was noted. Her past medical history was notable for a Hodgkin's disease (HD) at the age of 17 treated with heavy radiation therapy **(**>40Gy**)** and a left breast cancer at the age of 31 years old, treated by mastectomy and chemotherapy. Electromyography (EMG) revealed an acute radiculopathy in the right C5 and C6 territories. A first MRI of the right brachial plexus and of the cervical spine performed 7 months earlier was reputed normal but a second MRI revealed a tumoral mass arising from the brachial plexus, with an extraforaminal extension along the C5 and C6 roots (**Fig 1A**, arrow). Positon Emission Tomography (PET) of the whole body with fluorodeoxyglucose (FDG) showed an increased FDG uptake at the level of the lesion, with no sign of secondary localisation. Surgical biopsy of the subclavicular mass was performed and histology revealed a poorly differentiated malignant tumour. Its pattern was plexiform and characterized by multiple nodules separated by a connective tissue sheath (**Fig 1B**, HE, 25x) and containing malignant tumour cells admixed with residual axons (**Fig 1C**, HE, 400x), well demonstrated by their immunopositivity for the neurofilaments (**Fig 1D**). In immunohistochemistry, 10-20% of the tumour cells were positive for the S-100 protein (**Fig 1E**), 30% were positive for the CD56 (**Fig 1F**, 100x) and 10-20% positive for the epithelial membrane antigen (EMA). The proliferative index was very high with strong immunopositivity for the Ki-67 (**Fig 1G**). A diagnosis of Malignant Peripheral Nerve Sheath Tumour (MPSNT) of the brachial plexus was proposed. The patient is currently treated by chemotherapy and her surgical management is under discussion.

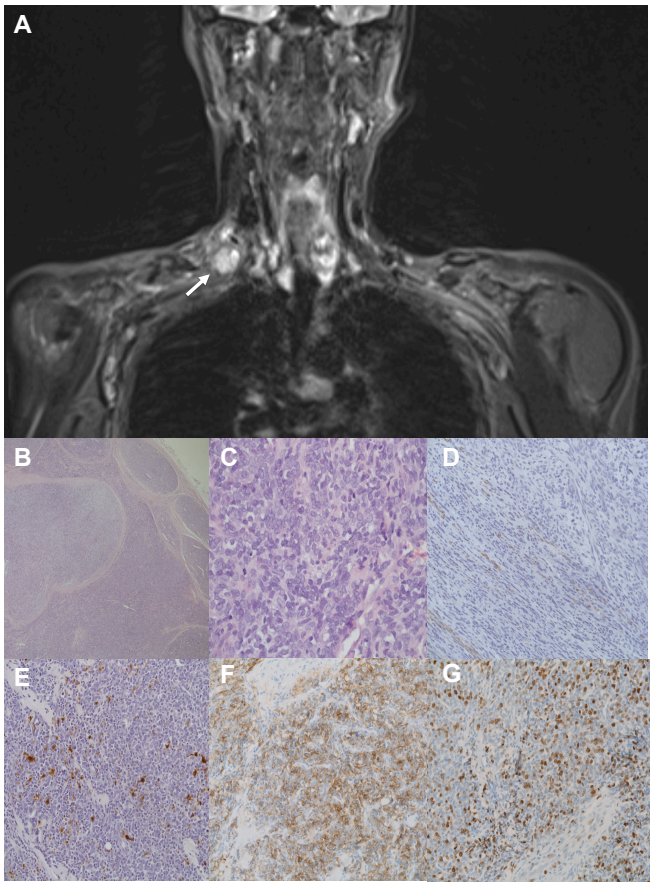

Figure 1

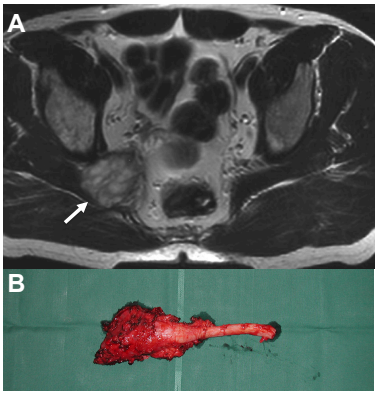

Figure 2

Case n°2 :

A 36 year-old man was referred for a history of right sciatic neuralgia that appeared 3 years earlier. The medical history of the patient was notable for a right seminoma at the age of 31 year-old, treated by orchidectomy and prophylactic external radiotherapy (24 Gy). The neurologic examination revealed a loss of sensation and weakness in the right L5 and S1 radicular territories and a right ankle hyporeflexia. The EMG was suggestive of a right proximal sciatic nerve chronic involvement and the MRI of the pelvis demonstrated a nodular mass at the level of the greater sciatic foramen (**Figure 2A**, arrow) that was enhanced after contrast injection. The mass was hypermetabolic on the PET-FDG, with no other focus of abnormal FDG uptake. A surgical biopsy was performed and the neuropathological findings were consistent with a heteregeneous tumour with mixt features of typical neurofibroma and atypical zones of hypercellularity with an increased mitotic index. Immunohistochemical analyses were not available. A diagnosis of low-grade MPSNT of the right sciatic nerve was proposed. Subtotal surgical resection was carried out. The tumor reccured after 10 months later and a new resection was undertaken (**Figure 2B**), followed by brachytherapy, external radiotherapy and chemotherapy. After 2 years, a third tumoral recurrence was observed and due to lack of tolerance to chemotherapy and major pain, the patient was admitted in the palliative care unit and died a few months later.

Conclusion and discussion

MPNSTs are rare tumors accounting for 3 to 10% of all tissues sarcomas[1]. Half of the cases described are sporadic, while the other half tend to appear in patients suffering from tumor prone conditions, such as neurofibromatosis type 1[2]. Although secondary neoplasms are known complications of radiotherapy, descriptions of peripheral nerve sheath tumors (PNST) are scarce in this context[3-6]. The exact pathophysiology of radiation-induced PNSTs remains unclear but vascular alterations, direct damages to axon or Schwann cell and nerve compression by soft tissue fibrosis are thought to play a role[7]. Although surgical removal sometimes followed by chemotherapy is the mainstay for the management of MPNSTs, they usually carry a poor prognosis[8]. Our 2 cases emphasize that the possibility of radiation-induced MPNST has to be kept in mind when investigating a localized neuropathy in a previously irradiated area.

References:

1. **Katz D, Lazar A and Lev D.** Malignant peripheral nerve sheath tumour (MPNST): the clinical implications of cellular signalling pathways. *Expert Rev Mol Med* 2009; e30.
2. **Brems H, Beert E, de Ravel T and Legius E.** Mechanisms in the pathogenesis of malignant tumours in neurofibromatosis type 1. *Lancet Oncol* 2009; **5**:508-15.
3. **Zadeh G, Buckle C, Shannon P, Massicotte EM, Wong S and Guha A.** Radiation induced peripheral nerve tumors: case series and review of the literature. *J Neurooncol* 2007; **2**:205-12.
4. **de Quintana-Schmidt C and Clavel Laria P.** Multiple radiation-induced neurofibromas. *Neurology* 2010; **13**:1214.
5. **Lai V, Wong YC, Poon WL, Fu YP, Lam TC and Yuen SC.** Radiation-induced peripheral nerve neurofibromata in a patient receiving hypofractionated radiation therapy. *AJNR Am J Neuroradiol* 2008; **10**:1995-7.
6. **Foley KM, Woodruff JM, Ellis FT and Posner JB.** Radiation-induced malignant and atypical peripheral nerve sheath tumors. *Ann Neurol* 1980; **4**:311-8.
7. **Pradat PF, Poisson M and Delattre JY.** [Radiation-induced neuropathies. Experimental and clinical data]. *Rev Neurol (Paris)* 1994; **10**:664-77.
8. **Moretti VM, Crawford EA, Staddon AP, Lackman RD and Ogilvie CM.** Early Outcomes for Malignant Peripheral Nerve Sheath Tumor Treated With Chemotherapy. *Am J Clin Oncol* 2010;

The authors have nothing to disclose