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Letter to the Editor

Chronic inflammatory polyneuropathy revealing malignant melanoma

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Introduction

In most instances, when chronic inflammatory demyelinating polyneuropathy (CIDP) is associated with cancer, it occurs in the setting of hemopathies, particularly those involving paraprotein. CIDP associated with malignant melanoma is exceedingly rare [1–3]. In two such cases, the neuropathy revealed the neoplasm. We here report a third case of CIDP revealing malignant melanoma which was strikingly indolent, as in the two previously reported cases, suggesting a strong anti-tumor reaction.

Case report

A 32-year-old man with no past history presented in June 2000 with paresthesias in both feet. In July 2000, the patient noticed a progressive lower limb weakness and complained of cramps after exercise. In September 2000, he experienced trouble using stairs or getting out of a chair and after 2 months was unable to walk unassisted. At first examination in November 2000, he exhibited moderate, mostly proximal lower limb motor deficit, but no objective sensory disorder though he complained of paresthesias in both hands and feet. Deep tendon reflexes were present except for the ankle jerks. Cranial nerves were normal. The CSF protein content was elevated to 363 mg/dl with eight white blood cells. Other laboratory studies were unremarkable, including viral serologies, notably HIV test, sedimentation rate, serum and urine immunoelectrophoresis with immunofixation, thyroid function tests, rheumatoid factor, anti-MAG antibodies, ANA. Electrophysiologic studies demonstrated prolonged distal motor latencies (especially marked in the lower limbs), prolonged F-wave responses with normal motor conduction velocities and no neuro-muscular junction block, suggestive of polyradiculoneuropathy. An MRI of the lumbar spine showed contrast-enhancement of the lumbar roots. General examination showed a 10 mm well-circumscribed red nodule below the right knee, which had first appeared 2 years previously and had been treated with liquid nitrogen but had relapsed after 1 year. A skin biopsy demonstrated the metastasis of an amelanotic malignant melanoma. The patient was treated with intra-venous immunoglobulins (IV Ig) for 5 days (0.4 mg/kg daily). In December 2000, the patient could walk unassisted, the paresthesias had disappeared, tendon reflexes were all present and a second IV Ig course was administered. In January 2001, the patient had fully recovered and declined further Ig treatment. In February 2001, enlarged right inguinal lymph nodes were noticed and removed. Pathological studies revealed malignant melanoma. No other skin lesions or vitiligo were found and search for other metastases proved negative. No further treatment was administered. At last follow-up on March 2004, the patient was free of both neurologic and melanomatous diseases.

Discussion

With only two published cases, melanomas revealed by CIDP are very rare [1]. Yet several lines of evidence suggest that the association is unlikely to be merely coincidental. Melanocytes and Schwann cells are of neuroectodermal origin and therefore share several cell surface antigens such as MAG and the gangliosides GM2, GM3, GD2 and GD3 [2,4]. Besides, demyelinating sensori-motor neuropathies have been reported in melanoma patients vaccinated with melanoma cell lysates or receiving monoclonal anti-GD2 antibody immunotherapy, then suggesting a cross-reactive mechanism with anti-GD2 antibodies targeting common antigenic determinants on melanoma cells and peripheral nerves [5–7]. The autoimmune hypothesis is further supported by the fact that the two patients reported by Bird et al. had vitiligo, an auto-immune disorder characterized by loss of melanocytes and frequently seen in the setting of melanomas [1]. Interestingly, this condition appears more frequent in slow growing neoplasms and is considered to reflect spontaneous anti-tumoral immunity [8,9]. Our patient and Bird's ones presented with vanished primary skin sites and long disease-free survivals without any treatment after surgery (2–4 years+) [1]. This strikingly indolent course is common to neurological paraneoplastic syndromes and here probably reflects a strong anti-tumor response.

References

1. Bird SJ, Brown MJ, Shy ME, Scherer SS: Chronic inflammatory demyelinating polyneuropathy associated with malignant melanoma. Neurology 46: 822–824, 1996
2. Weiss MD, Luciano CA, Semino-Mora C, Dalakas MC, Quarles RH: Molecular mimicry in chronic inflammatory demyelinating polyneuropathy and melanoma. Neurology 51: 1738–1741, 1998
3. Anthoney DA, Bone I, Evans TRJ: Inflammatory demyelinating polyneuropathy: A complication of immunotherapy in malignant melanoma. Ann Oncol 11: 1197–1200, 2000

4. Noronha AB, Harper JR, Ilyas AA, Reisfeld RA, Quarles RH: Myelin-associated glycoprotein shares an antigenic determinant with a glycoprotein of human melanoma cells. J Neurochem 47: 1558–1565, 1986
5. Fuller GN, Spies JM, Pollard JD, McLeod JG: Demyelinating neuropathies triggered by melanoma immunotherapy. Neurology 44: 2404–2405, 1994
6. Saleh MN, Khazaeli MB, Wheeler RH, Dropcho E, Liu T, Urist M, Miller DM, Lawson S, Dixon M, Russell CH, LoBuglio AF: Phase I trial of the murine monoclonal anti-GD2 antibody 14G2a in metastatic melanoma. Cancer Res 52: 4342–4347, 1992
7. Yuki N, Yamada M, Tagawa Y, Takahashi H, Handa S: Pathogenesis of the neurotoxicity caused by anti-GD2 antibody therapy. J Neurol Sci 149: 127–130, 1997
8. Duhra P, Ilchyshyn A: Prolonged survival in metastatic malignant melanoma associated with vitiligo. Clin Exp Dermatol. 16: 303–305, 1991
9. Yee C, Thompson JA, Roche P, Byrd DR, Lee PP, Piepkorn M, Kenyon K, Davis MM, Riddell SR, Greenberg PD: Melanocyte destruction after antigen-specific immunotherapy of melanoma: direct evidence of T cell-mediated vitiligo. J Exp Med 192: 1637–1644, 2000

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