Highly aggressive leiomyosarcoma associated with Lynch II syndrome: increasing the range of extracolonic cancers related with hereditary non-polyposis colonic cancer

Lynch syndrome, or hereditary non-polyposis colorectal cancer (HNPCC), is a hereditary syndrome that predisposes the individual to different types of cancer. The appearance of a colorectal cancer (usually in the right colon) at a young age is the guiding symptom [1]. Moreover, this can also be associated with other extracolonic cancers (mainly located in the endometrium, stomach, ovary, hepatobiliary tract and urinary tract) [2]. The syndrome is classified as Type I in the absence of extracolonic cancers and Type II if these are present. However, sarcomas have rarely been described in these families.

We report a 19-year-old woman admitted to the surgery unit of our hospital in November 1993 with an infiltrating lesion of the right paravertebral muscle tissue with irregular edges suggestive of a neoplasm. Pathological analysis and positivity for vimentin, actin and desmin by immunohistochemistry confirmed the diagnosis of pleomorphic leiomyosarcoma. The patient received local radiotherapy (50 Gy) and chemotherapy in the postoperative period as adjuvant therapy. In 1996, a lung and a cerebral metastasis were removed. The patient died in June 1997.

When the patient was first diagnosed, a family history of this syndrome was only known in the paternal grandmother. However, owing to the aggressive nature of the tumour and the patient’s young age a more detailed family study was carried out, which also detected a similar clinical background in the paternal grandfather that was ascribed to Lynch syndrome. It is interesting to note that both the maternal and paternal line on her father’s side meet Amsterdam criteria. Therefore, in our patient’s family background, two families with a high prevalence of tumours had converged (Figure 1).

Preliminary results of the analysis of the tumours on both sides of the family showed a high degree of instability of microsatellites (data not shown) confirming that both families are carriers of the syndrome. The two clinical family backgrounds, together with the early appearance of the tumour, allow us to establish an association between this tumour and Lynch syndrome, and rule out the possibility that this is a sporadic case of leiomyosarcoma in a family of carriers of Lynch syndrome. An extensive review of the literature confirms that there has been no previous reported case of a leiomyosarcoma associated with Lynch syndrome. Joseph-Reinete et al. [3] described the association between a gastric sarcoma and the syndrome, although in this case the immunohistochemical analysis of actin and desmin was negative. In contrast, in our patient both of these results were positive, clearly demonstrating the muscular origin of the tumour.

**Figure 1.** Family tree of the paternal grandmother known at the time of diagnosis of the tumour, and paternal grandfather discovered after diagnosis of the disorder. The arrow indicates the position of the patient in the family.

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According to current knowledge of the molecular genetics of sarcomas of soft tissue, the most common alterations occur in tumour suppressor genes and, to a lesser extent, in oncogenes. In contrast, microsatellite instability, a characteristic anomaly of tumours associated with Lynch syndrome, has rarely been described in sarcomas of soft tissues (2 of 216); indicating that the mutation of the underlying reparatory genes does not play an important role in sarcoma development [4].

The case reported here, therefore, increases the range of tumours associated with Lynch syndrome and emphasizes the importance of carrying out a detailed family study to identify these families. Especially since the studies by Järvinen et al. on the benefits of screening [5] and by Vansen et al. on the cost-benefit of screening [6], have demonstrated that close surveillance of families at risk significantly increases survival of the affected individuals.

V. Medina Arana1, Y. Barrios del Pino2, C. García-Castro3, J. J. González-Aguilera4, A. Fernández-Peralta4 & F. González Hermoso1

1Servicio de Cirugía General y Digestiva; 2Unidad de Investigación; 3Servicio de Anatomía Patológica, Hospital Universitario de Canarias, Ofra-La Cuesta, 38071 La Laguna, Tenerife; 4Unidad de Genética Dpto. de Biología, Universidad Autónoma de Madrid, 28049 Madrid, Spain (E-mail: vmedina@comtf.es)

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