Case Report

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ELEVATED SERUM S-100B LEVELS WITH NEGATIVE PET/TC AND CT-SCAN IN A METASTATIC MELANOMA PATIENT.

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SUMMARY

The incidence of melanoma is increasing worldwide. Prognosis for metastatic melanoma is poor; early detection of recurrent or metastatic disease may improve therapy strategies and survival. Several possible biomarkers for melanoma have been investigated. S-100B was found to be a sensitive and specific serological tumor marker; furthermore, its concentrations are correlated with the clinical stage of disease. Serum S-100B is also an independent prognostic factor for survival and can be used to monitor response to treatment. We present the case of a 55 year old woman, whose diagnosis of melanoma distant metastases was suggested by a progressive increase in serum S-100B levels, while other blood tests, physical exam and imaging techniques, including PET/TC and CT-scan, were negative. S-100B is currently the most accurate biomarker in melanoma patients; its role in the management of melanoma patients has been the object of study and it has been documented as a valuable independent prognostic factor. The case we present shows that S-100B levels may also be useful in the early detection of melanoma recurrences, even when imaging techniques are negative.

Introduction

The incidence of cutaneous melanoma is increasing faster than any other cancer in the United States. Overall, melanoma incidence has increased by 3,1% annually during the last 20 years. In 2007, the incidence rate in the United States was 27,5/100.000 in whites and 1,1/100.000 in blacks [1]. Prognosis for advanced and metastatic melanoma is poor, with a 5-year survival of 78%, 59% and 40% for patients with stage IIIA, IIIB and IIIC respectively, and a 1-year survival of 62% for M1a, 53% for M1b and 33% for M1c [2]. Early detection of recurrent disease and disease progression may improve therapy strategies and survival chances of patients with melanoma. Several possible biomarkers for melanoma have been investigated. Serum lactate dehydrogenase (LDH) has high specificity for melanoma, but low sensitivity [3]. Increased S-100B concentrations were first detected in melanoma patients in 1980 [4]. S-100B is a 21 kilodalton protein of neuroectodermal and mesodermal origin expressed in various parts of the body, including melanoma cells. Serum S-100B can be measured using an immunoradiometric assay or with immunoluminometric assay. S-100B was found to be a sensitive and specific serological tumor marker for melanoma; the proportions of patients with elevated S-100B concentrations were 0-9% in stage I/II, 5-98% in stage III, and 40-100% in stage IV melanoma [3]. Serum S-100B concentrations are therefore correlated with the clinical stage of disease. Increased S-100B concentrations are an expression of disease progression, whereas successful treatment with surgery, chemotherapy and immunotherapy are associated with decreased concentrations [5]. A cut-off point of 0,15 g/L as UNL was established by feasibility studies performed by the manufacturer using the cheminluminescence assay

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Table 1: Serum S-100B levels

Date (dd/mm/yy)	S-100B (g/L)
19/02/09	0.10
23/04/09	0.13
30/07/09	0.11
29/10/09	0.10
26/03/10	0.17
02/07/10	0.29
07/09/10	0.32
19/10/10	0.41
21/12/10	0.09
28/01/11	0.09
16/02/11	0.10

LIAISION Sangetc 100 [6]. A rise in the level of S-100B during follow-up has been reported to have high sensitivity and specificity for recurrence of disease irrespective of its location. Serum S-100B is also an independent prognostic factor for survival: in stage IV patients, a normal S-100B indicates a relatively good prognosis, while an elevated level indicates a poor prognosis [5]. Serum S-100B is also used to monitor response to treatment [7]. Additional testing to confirm the prognostic value of S-100B is planned as part of ongoing (ECOG 1697) and planned studies of adjuvant therapy in melanoma.

Case Report

We present the case of a 55 year old woman, whose diagnosis of melanoma distant metastases was suggested by a progressive increase in serum S-100B levels, while other blood tests, physical exam and imaging techniques, including PET/TC, were negative. All S-100B levels are chronologically listed in Table 1. The progressive rise in serum S-100B levels from 23rd March 2010 and 19th October 2010 corresponds with the appearance and growth of the secondary lesion; the last values, which are under the upper normal level, were detected after surgical removal of the distant metastases.

The patient has familiarity for breast and lung cancer. She is neither a smoker nor a drinker. Her remote pathological anamnesis is negative for relevant pathologies.

On 14th April 1994 she was diagnosed with left shoulder cutaneous melanoma (Breslow 1,5 mm; Clark IV; ulcerated). She underwent a wide excision on 3rd May 1994 and she was followed-up by Genoa IST Oncology Unit until December 1997. No clinical or instrumental exam suggested recurrences in that period.

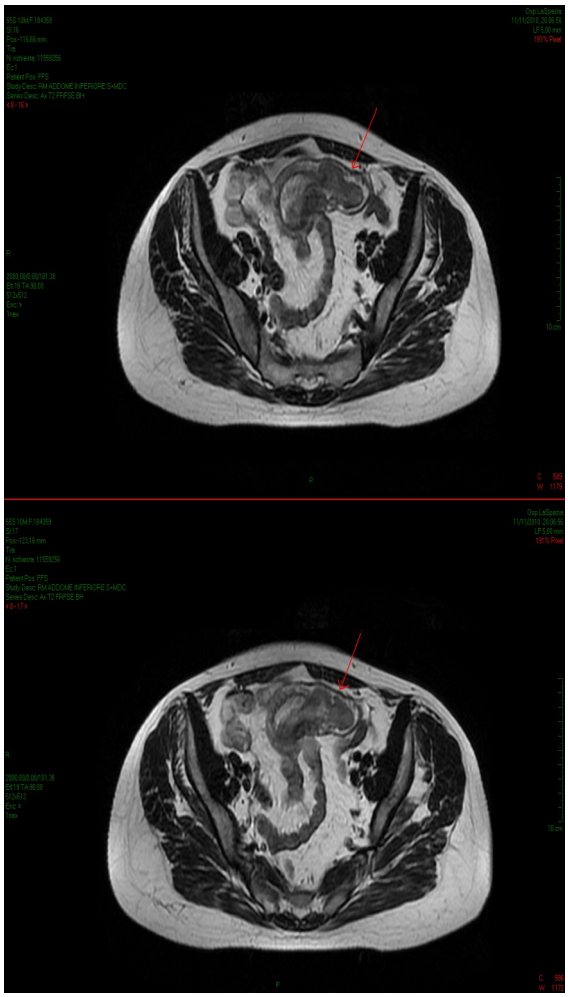
In December 2008 she presented left axillary lymphadenopathy. On December 18th she underwent a needle aspiration: as the cytological exam was positive for atypical cells, a surgical intervention was scheduled. On 20th January 2009 she underwent radical left axillary dissection: 3 out of the 17 lymph nodes removed were positive for melanoma recurrence.

The patient started a low-dose adjuvant IFN treatment (3 MUI three times a week). A 3-month follow-up was scheduled: each visit included a physical exam and blood tests (hemochrome, liver and kidney functions, LDH and S-100B); chest X-ray and abdominal-US were performed every 6 months.

On 26th May 2010 a 0.17 g/L level of S-100B was noticed: the physical exam was negative and no previous blood test, chest X-ray or abdominal-US were suggestive of melanoma recurrence. A PET/TC and CT-scan of chest and abdomen were negative for metastatic disease. On 2nd July 2010 the S-100B level rose to 0,29 g/L. She presented bilateral inguinal lymphadenopathy, but the needle aspiration was tumor-negative. Furthermore, a colonoscopy was scheduled: it was normal. On 7th September and 19th October the S-100B levels were 0,32 and 0,41 g/L respectively. Another PET/TC and CT-scan were performed but they were negative. Finally, an abdominal-MRI was performed, showing a 2-cm lesion (suggestive for polyp) at the end of a 10-cm ileo-ileal invagination (Figure 1). On 19th November 2010 a 10-cm ileal resection was performed: the histopathological exam of the lesion revealed a 5-cm melanoma metastasis (S-100+, MART-1+, 10 mitosis/mm^2). After one month, the S-100B levels were under the upper normal limit (0,09 g/L).

On January 24th a CT-scan of the brain, chest and upper and lower abdomen confirmed the absence of distant metastases

Figure 1: The red arrows show the lesion in two sequential T2-weighted MRI images.



and the S-100B levels were still under the UNL.

Conclusions

S-100B is currently the most accurate biomarker in melanoma patients and its role in the management of melanoma patients has been the object of study. An elevated S-100B level in clinical stage III melanoma patients is associated with decreased disease-free survival [3]. Furthermore, the S-100B level is an independent prognostic factor in stage II and III patients. In stage IV patients, a normal S-100B level indicates a relatively good prognosis, while an elevated level indicates a poor prognosis. Serum S-100B is also used to monitor response to treatment in stage IV patients [5].

The case we have presented shows that S-100B levels may also be useful in the early detection of melanoma recurrences, even when imaging techniques are negative. Elevation of S-100B in melanoma patients is a highly specific indicator of recurrence. Therefore, other than a prognostic factor, S100-B may be useful as a complementary diagnostic technique in the management of melanoma patients.

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