Melanoma is the sixth most common cancer in the United States, and its incidence rates are currently increasing faster than for any other cancer. Nodular melanoma often carries a poor prognosis because of local invasion and early distant metastasis. Herein, we report a case of the largest primary melanoma in the current literature, along with the management strategy of a primary tumor of this magnitude.

Melanoma is the sixth most common cancer in the United States, and its incidence rates are currently increasing faster than for any other cancer [1, 2]. In 2001 the lifetime risk of melanoma increased to approximately 1 in 71, compared with 1 in 150 in 1985 and 1 in 600 in 1960 [2]. It is estimated that during the year 2006 this lifetime risk figure will increase yet again to (or slightly below) 1 in 50 people and that there will be over 62,000 new cases of melanoma diagnosed in the Untied States [3]. Nodular melanomas (NM) comprise 7-10 percent of all melanomas at present and are the second most common subtype of malignant melanocytic neoplasm, next to superficial spreading melanoma [4]. Major risk factors for NM include the presence of multiple dysplastic nevi, positive family history, light colored skin with an inability to tan, and excessive sun exposure [4].

Nodular melanoma often presents as an expanding darkly pigmented cutaneous nodular lesion, usually found on the sun exposed areas of the skin, with far fewer such lesions occurring in covered areas. The most common sites are the trunk in men and the legs in women [4]. The lesion is usually asymmetric with irregular borders, but it may also present as a round to globoid exophytic mass of varying size. Because much of the pigmentation of such lesions is often the result of blood rather than melanin, the differential diagnosis may be between a pigmented tumor, such as NM, or a vascular neoplasm [5]. The most important prognostic factor with respect to primary cutaneous melanoma is Breslow thickness. Nodular melanoma is known to present with greater thickness than the other subtypes of melanoma; therefore, it often carries a more ominous prognosis. One study showed that during a 10-year period, only 3 percent of NM presented as thin lesions (< 3mm) [6]. In a histopathological reassessment of nodular melanoma, Weyers et al. found the mean Breslow thickness to be 4.01mm with a standard deviation 2.42mm [7]. We report herein a patient who developed a striking nodular melanoma that was 54mm thick at presentation.

Clinical synopsis

The patient is a 29-year-old man, in previous good health, who reported having a hyperpigmented area on his lower back since childhood, presumed to be a benign congenital nevus. This macular lesion measured approximately 2-3cm in diameter without clinically obvious lateral expansion or vertical growth until 1 year prior to presentation. At that time, the lesion became progressively larger and ulcerated, with a dramatically rapid increase in growth during the final 2 months before the patient sought medical attention.

The patient complained of intermittent shooting pain radiating from the area. He complained also of fatigue, night sweats, fever, and an unexpected 30 lb weight loss during the preceding 8 months. He had no significant past medical history; however, he had a positive family history of metastatic melanoma in his paternal grandfather.

Physical examination revealed a fair-complected man with no abnormalities aside from a yellowish-brown mass located on the lower back measuring 22 x 25 x 7 cm with an area of central necrosis measuring 13.0 x 12.5 cm, and an enlarged left inguinal lymph node. The mass was a malodorous, fungating growth, with areas of central necrosis and evidence of recent infarction and bleeding. (Figs. 1-2).

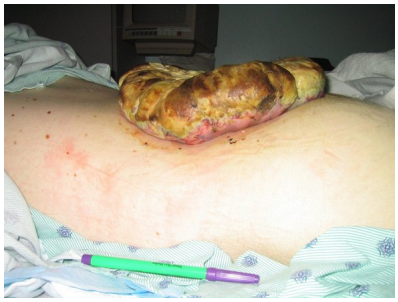

Figure 1. Gross appearance of primary melanoma: height 5.4cm

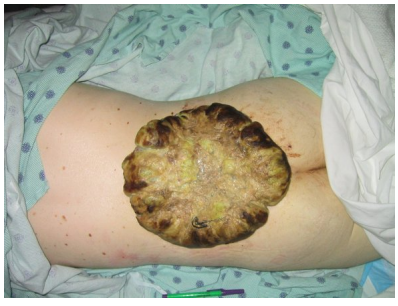

Figure 2. Gross appearance of primary melanoma: width 25.0x20cm

The CT imaging disclosed mass extension into the subcutaneous tissues (Fig. 3), along with evidence of metastasis in a left inguinal lymph node measuring 15cm. Tiny pulmonary nodules were suspicious for metastasis, but biopsy confirmation was unattainable given their small size. Biopsy of the primary tumor revealed a high-grade, poorly differentiated malignant neoplasm consistent with nodular malignant melanoma (Fig. 4). The tumor was S-100 positive, MART-1 negative, and rarely HMB-45 positive. According to current staging criteria, the patient was classified as stage-IV disease.

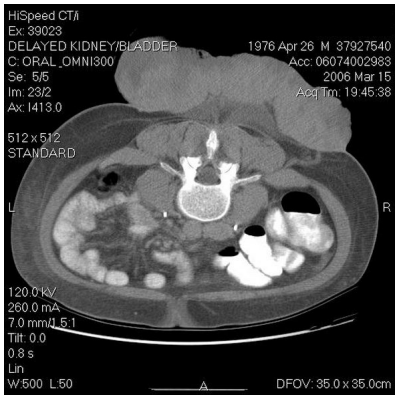

Figure 3. CT image shows mass extension into subcutaneous tissues

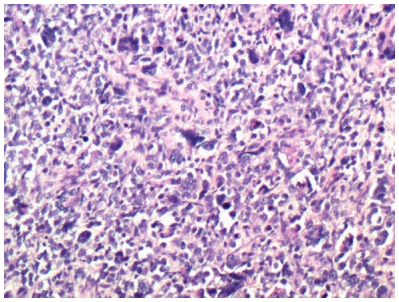

Figure 4. High grade melanoma with poor differentiation

Palliative debulking was performed by local excision with a 4-cm margin. During the surgical excision, there was no gross visual evidence of tumor extension beyond the subcutaneous tissue. The total mass, including margin of excision, was 7280 grams. The mass had a superficial layer of yellow fibrino-purulent exudate averaging 1.1 cm in thickness. The tumor was variable in color with focal areas of hemorrhage and cystic degeneration. After excision of the primary tumor, the remaining tissue was irrigated and placed under a wound vacuum to encourage granulation. Skin grafting was performed 7-days post-operatively. In this particular case, surgical intervention was palliative in nature, designed to ease the patient's discomfort and reduce the risk of serious superinfection.

After the graft was allowed to properly heal, the patient received chemotherapy. His large left inguinal lymph node (measuring 15cm) was used to judge clinical response. He first received 1 course (6 weeks) of temazolamide with no response. He subsequently received a course of temazolamide combined with cisplatin, again with no response. In fact, he had disease progression evident by further growth of his inguinal lymph node. The chemotherapeutic regimen was changed to paclitaxel, cisplatin, and temazolamide. Following two rounds of this combination chemotherapy, his left inguinal lymph node has decreased from 15cm to 6cm by exam, indicating significant clinical response.

Discussion

Despite many surgical and chemotherapeutic options for the treatment of metastatic melanoma, no consensus has been reached as to the optimal management. Traditionally, management of melanoma metastatic to distant sites involves either a single-drug or multi-drug chemotherapeutic regimen. However, complete response (CR) rates have been poor (< 6 %) with a minimal increase in the median survival [8, 9, 10].

Surgical intervention has also been considered in the management of these patients, although it should be clear at the outset whether the goal of surgery is palliative or potentially curative. Data suggests that if surgical intervention is palliative for specific symptoms, then more than 75 percent of patients will be treated successfully depending on the resection site and symptomatology. Palliative surgery results in minimal morbidity and operative mortality. However, if the goal of surgical resection is curative, then only those patients with a high likelihood of improved postoperative survival should be selected on the basis of favorable disease biology [11]. Recent series have demonstrated 5-year survival rates of 20-27 percent following pulmonary metastasectomy and 28-41 percent following complete resection of gastrointestinal metastases [5,12, 13, 14]. Similarly, significant survival rates have been reported for patients with subcutaneous or distant nodal metastasis after resection [15, 16]. In all of these reports, patients rendered disease-free by surgical resection fared better than those

undergoing incomplete surgical resection or nonoperative management.

At the time this report was written, our patient had undergone palliative surgery along with postoperative multidrug chemotherapy. At the present time, he is showing objective disease regression on taxol, cisplatin, and temazolamide. However, as is the usual case with metastatic melanoma, it remains to be seen if this disease regression will translate into increased survival.

After extensive review of the literature, we believe this case represents the largest primary melanoma described in the readily available medical literature. The largest primary melanoma published prior to this case measures 16cm [17]. A larger melanoma measuring 35 x 29 x 25cm has been reported; however, it represents a metastatic lesion [18]. It is difficult to explain how some patients with much smaller primary lesions fair so poorly with early distant metastasis, while others, such as our patient, develop very extensive primary lesions without metastasis or with only late metastatic disease. Cases such as these remind us how little we truly know about the biological behavior of melanoma and the patient's inherent immunological response to the tumor. Considerable opportunity remains for research in this area and subsequent treatment development based upon this investigation.

Mandy Harting MD[1], William Tarrant MD[2], Craig A Kovitz MD[3], Ted Rosen MD[1], Matthew T Harting MD
2
, Eduardo Souchon MD
2

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1. Baylor College of Medicine, Department of Dermatology, Houston, Texas2. University of Texas Medical School at Houston, Department of Surgery, Houston, Texas 3. University of Texas M.D. Anderson Cancer Center, Department of Melanoma Oncology, Houston, TX

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