Gastrointestinal Bleeding as Initial Presentation of Melanoma of Unknown Primary Origin: Report of a Case and Review of the Literature

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Abstract. The case of an 81-year-old patient, initially presenting with gastrointestinal (GI) bleeding, including melena and hematemesis is reported. Endoscopy revealed an ulcerated mass of the stomach corpus with immunohistochemistry stains consistent with metastatic melanoma. The thorough physical and paraclinical examination did not reveal any lesions or nodules as a primary site of the disease. The literature concerning this rare presentation of melanoma is also reviewed.

Malignant melanoma incidence is rapidly growing worldwide. A total of 62,480 new cases are expected in the United States in 2008 and 8,420 patients will eventually succumb to their disease the same year (1). However, the presence of metastatic melanoma without an identifiable primary lesion, the so-called melanoma of unknown origin is very low (<5%). Its biological behavior seems similar to the cutaneous melanoma, with the sites of metastasis being the most important determinants of its clinical course and prognosis (2-6). The pathogenesis of this unusual presentation of melanoma can be a result of a previously existing clinically or histologically misdiagnosed skin lesion, spontaneously regressed primary melanoma, or de novo malignant transformation (7, 8).

The gastrointestinal (GI) tract is a favored melanoma metastasis (9). In 60% of patients who died of disseminated melanoma, the GI tract was affected, while only 1% to 4% of GI metatases were clinically diagnosed ante mortem (10).

The most common sites of invasion, by order of frequency include the liver, small intestine, colon and stomach (11-13). Information regarding GI bleeding as the initial incident of melanoma gastric invasion is very limited. Herein, such a presentation of melanoma of unknown origin, treated in our department, with GI bleeding being the initial presentation is reported.

Case Report

The 81-year-old male patient presented with melena and hematemesis, with no previous history of GI bleeding. He underwent upper GI endoscopy, which showed a large ulcerated volcano-like tumor located at the stomach corpus near the greater curvature, as the source of the haemorrhage (Figure 1A and B). Endoscopic hemostasis was achieved with adrenaline and high doses of PPI’s (Figure 1C and D). Four days later, a biopsy from the ulcer’s rib revealed segments of mucosa infiltrated by metastatic melanoma. Immunohistochemistry stains showed neoplastic cells positive for HMB-45, S100 protein and vimentin and no staining for keratin, immunohistochemical pattern consistent with melanoma lesions. The chest and abdomen CT scans uncovered dissemination of the disease, with lesions consistent with metastases in both lungs and adrenal glands. Moreover, enlarged iliac lymph nodes (2-3 cm) were noticed. Despite the careful physical and paraclinical examination, no suspicious skin lesions were discovered. The patient is currently being treated with high doses of interferon-alpha.

Discussion

The incidence of melanoma of unknown origin is very low. From the analysis of the National Cancer Data Base (NCDB) in the US for the period 1985-1994, encompassing 84,836 cases of melanoma only 2.2% were identified as melanoma with unknown primary origin (5). Similarly, among 2,485
melanoma patients seen in Massachusetts General Hospital and Dana-Farber Cancer Institute, only 65 (2.6%) had melanoma with unknown origin (6). Other authors have raised that ratio to 4-6% (2-4). It occurs more often in men and is more common in the fifth and sixth decade of life (4, 6).

At presentation 60-65% of the melanoma patients have metastases to the lymph nodes. The remaining 35-40% present with disseminated disease including most frequently the lung, liver, brain, bone and adrenal glands. The neoplasm shows a predisposition to invade the axillary (25-54%), head and neck (21-32%), trunk (13%), and groin (7-24%) nodes (2-4, 14-15). The 5-year survival rate for patients, who initially have disease limited to the lymph nodes and treated with radical lymphadenectomy, varies from 29% to 59%.

On the contrary, patients with visceral metastases die approximately 6 months after diagnosis. The clinical disease course of patients with melanoma of unknown origin was equivalent to that of patients with primary skin melanoma, when the same clinical stages of the disease were compared (3, 4, 6, 16, 17). It is remarkable that geriatric patients with melanoma have a poorer prognosis than younger ones. This is influenced by the fact that the elderly tend to present with a more advanced stage (18).

Melanoma of unknown origin and skin melanoma are usually spread to the GI tract. In a large review of autopsies, the most frequent sites of GI invasion were, the liver (58-68%), the small bowel (35-58%), the colon (14-31%) and the stomach (5-22%) (9, 13). From the 4,600 melanoma cases of two large studies, only 7% of them were identified with gastric metastases (12, 19). Melanoma though, is associated with the highest rates of gastric metastases, compared to other solid neoplasms, such as lung and breast cancer (20, 21).

Endoscopy is the main procedure for the diagnosis and local treatment of melanoma gastric metastasis. Multiple submucosal nodules, ulcerations or polypoid mass can be observed. Barium swallow examination reveals polypoid or target lesions. The most characteristic is the bull’s-eye appearance, when the barium fills a central ulcer in a metastatic nodule (22-25).

Most typically gastric metastases induce abdominal pain, fatigue, weight loss and anemia, with a short history of a few months duration (22-24). Nevertheless, GI hemorrhage with melena and hematemesis should also be considered as a sign of gastric invasion (26). It seems that patients with metastatic disease to the stomach could benefit from aggressive radiological and endoscopic procedures for diagnosis and staging. The available literature offers information concerning the treatment of GI metastases from melanoma, but not particularly for gastric metastases. It is difficult to evaluate the data, when organs other than the stomach (liver, small intestine, colon, oesophagus) are involved. Palliation of the symptoms was achieved in 90% of all cases of GI lesions and mortality was low (3%) (27, 28). Gastrectomy is the standard treatment for metastatic lesions to the stomach, when possible. It is recommended for palliative or curative reasons, with significantly low mortality. Patients with gastric metastases may benefit from

Figure 1. Endoscopic findings of the patient presented with gastrointestinal bleeding: the gastric ulcer at diagnosis while bleeding (1 and 2), four days post hemostasis when biopsy was performed (3 and 4).
surgery if all macroscopic disease can be removed (10, 29, 30). An Italian study, which included 31 patients with gastric metastases of melanoma reported a survival of 21.6 months for those who underwent radical surgery. On the other hand, the patients without surgical excision of the tumor had a survival of only 3.6 months. Median survival was 14.2 months (19).

With regard to the reported case, it is of particular interest that the patient was asymptomatic prior to the GI bleeding, regardless of the advanced stage of his malignancy. The hemorrhage was successfully stanched, with no bleeding reported thereafter.

Conclusion

Melanoma of unknown origin is rare, with its clinical course, biological behavior and prognosis similar to the skin melanoma. The treatment of melanoma of melanoma of unknown origin should be chosen with the same criteria as used for cutaneous melanoma. Secondary tumors of the GI tract are unusual but are probably more common than clinically suspected and gastroenterologists should always bare that possibility in mind, when bleeding of the upper GI tract is investigated.

References


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