www.jmscr.igmpublication.org
Impact Factor 5.244
Index Copernicus Value: 83.27
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: http://dx.doi.org/10.18535/jmscr/v4i8.87

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Metastatic MalignantMelanoma of Gastrointestinal Tract with Unknown Primary- A Diagnostic Dilemma?

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ABSTRACT
Background: *Malignant melanoma with its diverse histological patterns and varied manifestations is a diagnostic enigma. This problem becomes even more complex when it presents as a metastatic lesion with no known primary site. This is referred to as malignant melanoma of unknown primary (MUP). MUP generally accounts for 2-9% of all melanomas [(1)]. The incidence of malignant melanoma in the gastro-intestinal tract without any evidence of a primary lesion in the skin or any other site is extremely rare [(2, 3)]*
Case: *We present here a case of a 58 yr old man with symptoms such as vomiting,epigastric pain and loss of appetite for two months. General examination revealed a right inguinal lymphadenopathy and hepatomegaly with no abnormality in skin. On endoscopic evaluation we found, multiple melanotic patches on gastric mucosa, .Metastatic melanoma in stomach with unknown primary is a rare entity and we report it here for documentation.*
Conclusion: *Metastatic malignant melanoma of the gastrointestinal tract without an identifiable source is exceptionally rare. The present case puts light into the extensive search and timely diagnosis to yield a early pre-mortem diagnosis and timely intervention.*
Keywords: *MUP, Gastric Melanoma, Diagnosis.*

INTRODUCTION

Malignant melanoma with its variable histological patterns and manifestations poses a diagnostic problem. This problem is aggravated when it presents as a metastatic lesion with no known primary site. This is referred to as malignant melanoma of unknown primary (MUP). It was first described in 1952 by Pack et al. and Dasgupta et al. first proposed the diagnostic criteria for this. MUP generally accounts for 29% of all melanomas [1]. Malignant melanoma in the gastrointestinal tract without any identifiable primary lesion in the skin or any other site is extremely rare [([2],[3])]. Such metastases are diagnosed in only 1.5% - 4.49% of

the patients premortem because they are usually asymptomatic [4],[5],[6].

CASE

A 58 year Muslim male presented to us with complains of vomiting off and on, epigastric pain, weight loss and anorexia for two months. On general examination he had pallor and right inguinal lymph node 2cm×1.5cm fixed, firm and non-tender. Chest, CVS and CNS examinations were within normal limit. On per-abdominal examination there was mild tenderness in epigastrium but no organomegaly or ascites. Bowel sounds were normal. Oro-genital system examination revealed no abnormality. Bio-chemical investigations were within normal limit except anemia (Hb-8gm%) and raised SGOT and Alkaline Phosphatase. Upper GI endoscopy was done and it revealed multiple black patches and sessile polyps with dark overlying mucosa in the body of stomach.(Fig.1)

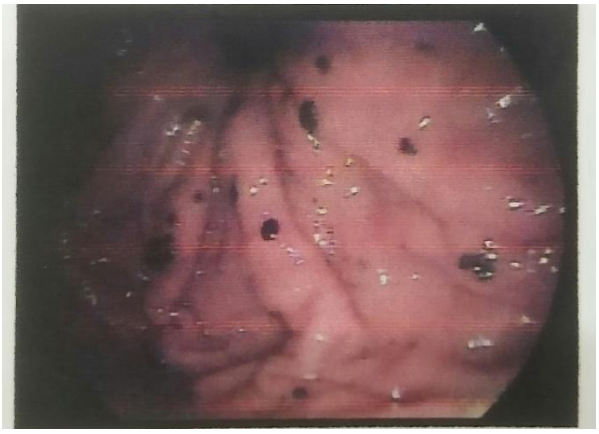

Fig – 1. - Upper gastrointestinal endoscopy showing multiple dark melanotic patches all over the Gastric mucosa

Endoscopic Biopsy showed neoplastic cells with brown pigments and surrounding benign gastric mucosa suggestive of a metastatic malignant melanoma. (Fig.2) The surrounding gastric mucosa was normal. Immuno-histochemistry of tumour cells showed cytoplasmic HMB-45. (Fig.3)

On Ultrasonography of abdomen and pelvis there were multiple hepatic metastasis, enlarged periportal nodes and Bull's Eye lesion in left adrenal. Fine needle aspiration cytology of the inguinal node showed metastatic melanoma

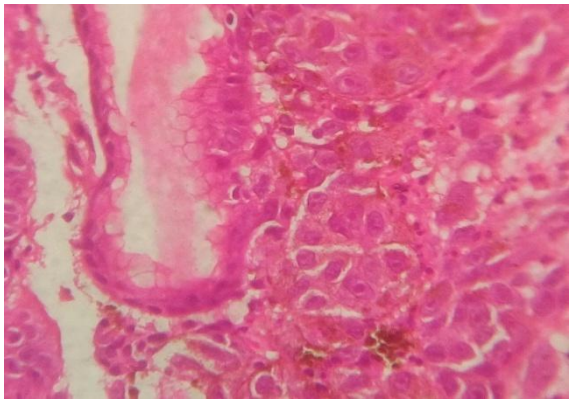

Fig. 2 - Endoscopic biopsy shows dark melanin pigments indicative of metastasis with adjacent normal gastric mucosa.

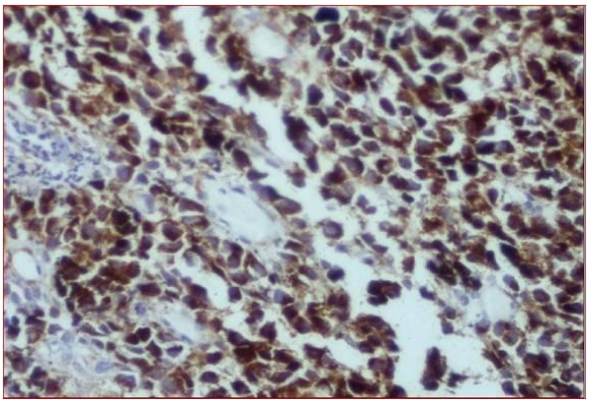

Fig. 3 – Immune-histochemistry shows HMB45 Expression

Extensive search for whole body skin didn't reveal any hypo or hyper-pigmented macules, papules, patches or melanotic naevi. The patient was further evaluated by Ocular examination (Direct and Indirect Ophthalmoscopy) and Otolaryngology examination but found to be normal. Patient underwent Colonoscopy and barium follow-through but no significant abnormality detected in small and large intestine. So the case was diagnosed as Metastatic Melanoma of Stomach, liver, adrenal and multiple lymphadenopathies with unknown primary. Patient was staged as stage 4 disease according to M.D Andersons staging classification. He was given supportive care and he deferred any kind of treatment further. After 3 weeks the patient died.

DISCUSSION

GI tract malignant melanoma is an uncommon entity which presents as a diagnostic dilemma of

whether the lesion is primary or secondary. It can be present starting from mouth to anus but the most common site is the small intestine [7]. Blecker et al. proposed a criteria for stamping the melanotic lesion as primary in the intestine if there was presence of only solitary lesion with no associated lesion in the skin and absence of intramucosal melanocytic lesion in the overlying or adjacent intestinal epithelium.[7] Mishima et al. proposed that the primary melanoma of the small intestine probably arises from the schwannianneuro blast cells associated with the autonomic innervations of the gut.[8] There is another school of thought that the melanoma arises from the melanoblastic cells of the neural crest which migrate to the distal ileum through omphalo-mesenteric canalor in APUD cells.[9] In our case the presence of multiple lesions in the intestine excludes the possibility of it being a primary lesion according to Becker's criteria.

Incidence of Melanoma with an unknown primary (MUP) is between 2% to 9% in literature. Armando et al., found the incidence of an unknown primary melanoma at 5.6% in there large series. The most common site of metastasis of MUP was lymph nodes with around 61% incidence and the rest had other disseminated sites of metastasis.[10] Metastasis in Bowel and liver was reported only in 7% of cases. In another series of 40 patients with an MUP Malignant melanomas account for 1 to 3% of all malignant lesions of the gastrointestinal tract. [7] The vast majority of gastrointestinal melanoma is metastatic from a cutaneous primary or they may originate from retina, anus and nail bed.[11] However, melanoma can arise spontaneously from within certain areas of the GI tract [12] and may sometimes be confused with rectal polyp.[13] Among metastatic melanoma, 65% had lymph nodemetastases alone and 28% had visceral lesions. [14] Another series finds the incidence of MUP to be 2.6% with lymph nodes being the most common site of metastasis. [15] The incidence of visceral metastasis alone in MUP is quite uncommon in all the reported series.

These tumours were first extensively investigated in 47 patients by Das Gupta et al. The criteria proposed by this group for the diagnosis of melanoma of unknown primary have been universally accepted till date. The exclusion criteria to diagnose MUP proposed by them are, history of previous orbital exenteration and history of excision, cauterisation or desiccation of any skin lesion with possibility of harbouring a melanoma like a birth mark, freckle, moleor other lesions. There should be a thorough examination of the anogenital region of the patients along with ophthalmoscopy to rule out any disease in those sites. [16] Upper airway and lower gastrointestinal examination, Computer Tomography of thorax and abdomen, USG of palpable lymphadenopathy, and cranial CT or magnetic resonance imaging should be done before reaching the diagnosis of malignant melanomas of unknown origin [17].

The patient included in our study fulfilled all the exclusion criteria of MUP after a thorough history, clinical examination and laboratory investigations as mentioned. The histopathological examination of the gastric biopsy was also consistent with the diagnosis of metastatic melanoma.

GI metastatic melanoma are present in more than 25% of patients with melanoma at autopsy but only 1-4% are diagnosed with metastatic melanoma of the GI tract with a known melanotic lesion.[18] Melanoma has a special affinity for metastasis to small bowel may be due to the presence of a chemokine CCR9 on human melanotic cells. It acts as a homing receptor for melanoma on small bowel. It also enhances the motility of the melanoma cell and its ligand CCL25. This CCL 25 is strongly expressed in the small bowel.([19],[20])

Four different types of metastatic melanoma of the small bowel have been described by Bender et al. Those are cavitary, infiltrating, exoenteric, and polypoid [often called a target or bull's-eye lesion. It is very difficult to differentiate between these four different types some times. In addition, they may be amelanotic at times.[21] Metastatic intestinal melanoma developing after spontaneous regression of a primary cutaneous melanoma shows the signs of chronic inflammation in the form of lymphocytic infiltration with melanophages, fibrosis and vascular

proliferation of the dermis histologically.[22] It is very difficult to distinguish between primary intestinal melanoma and metastatic intestinal deposits on the basis of histopathologic features alone.[23]

Several other possible aetiologies explaining MUP have been postulated: (1) the most widely accepted theory is of an antecedent, unrecognized, spontaneously regressed primary melanoma (2) histologically misdiagnosed previous lesion; (3) unrecognized concurrent melanoma; and (4) spontaneous malignant transformation of an isolated melanocytes. [16] Patients with an MUP and with a known primary with metastatic lesion in the same stage have similar overall survival and prognosis. [10] However, patients with an MUP with only lymph node metastases have been reported to have a better overall survival than patients with a known primary and lymph node disease in some series.[14] Patients having visceral metastasis especially GI and/or liver metastases usually have disseminated disease and a worse median survival in the range of 2 and 4 months. [24]

CONCLUSION

Metastatic malignant melanoma of the stomach without an identifiable source is exceptionally rare. Distinction of this entity from the primary lesion in the GI Tract presents as a clinical dilemma. Since the disease has a very bad prognosis, the importance of timely diagnosis is crucial but delayed presentation and low detection yield of the disease from the available investigations pose a clinical dilemma for its early and pre-mortem diagnosis. A high index of suspicion and appropriate requisite investigations with proper immunohistochemistry are required to reach an accurate diagnosis.

REFERENCE

1. Milton CW, Lane Brown MM, Gilder M, Malignant melanoma with an occult primary lesion, Br J Surg, 1967, 54(7):651–658
2. Sorensen YA, Larsen LB. Malignant melanoma in the small intestine. Ugeskr Laeger 1998; 160(10): 1480-1481.
3. Christova S, Meinhard K, Mihailov I, Alexiev B. Three cases of primary malignant melanomas of the alimentary tract. GenDiagnPathol. 1996; 142(1): 63-7.
4. Kadivar TF, Vanek VW, Krishnan EU. Primary malignant melanoma of the small bowel: a case study. Am Surg1992; 58: 418-422
5. Avital S, Romaguera RL, Sands L, Marchetti F, Hellinger MD. Primary malignant melanoma of the right colon. Am Surg 2004; 70: 649-651
6. Ollila DW, Essner R, Wanek LA, Morton DL. Surgical resection for melanoma metastatic to the gastrointestinal tract.Arch Surg. 1996 Sep;131(9):975-9; 979-80
7. Blecker D., Abraham S., Furth E.E., Kochman M.L. Melanoma in the gastrointestinal tract. American Journal of Gastroenterology. 1999Dec;94(12):3427–3433.
8. Mishima Y. Melanocytic and nevocytic malignant melanomas: cellular and subcellular differentiation. Cancer. 1967;20:632–649
9. Amar A., Jougon J., Edouard A., Laban P., Marry J.P., Hillion G. Primary malignant melanoma of the small intestine. Gastroenterologie Clinique et Biologique. 1992;16:365–367.
10. Giuliano AE, Moseley HS, Morton DL. Clinical aspects of unknown primary melanoma. Ann Surg. 1980;191:98–104.
11. Atmatzidis KS, Pavlidis TE, Papaziogas BT, Papaziogas TB. Primary malignant melanoma of the small intestine: report of a case. Surg Today. 2002;32:831–833
12. Manouras A, Genetzakis M, Lagoudianakis E, Markogiannakis H, Papadima A, Kafiri G, et al. Malignant gastrointestinal melanomas of unknown origin: Should it be considered primary? World J Gastroenterol. 2007;13(29):4027–4029.
13. Avital S, Romaguera RL, Sands L, Marchetti F, Hellinger MD. Primary

malignant melanoma of the right colon. Ann Surg. 2004;70:649–51.

14. Anbari KK, Schuchter LM, Bucky LP, Mick R, Synnestvedt M, Guerry D 4th, et al. Melanoma of unknown primary site: Presentation, treatment and progress: A single Institution study. Cancer.1997;79:1816–21.
15. Katz KA, Jonasch E, Hodi FS. Melanoma of unknown primary: Experience at Massachussets general hospital and Dana Farber cancer institute. Melanoma Res. 2005;15:72–82.
16. Dasgupta T, Bowden L, Berg JW: Malignant melanoma of unknown primary origin. Surg Gynecol Obstet 1963, 117: 341-345
17. Schlagenhauff B, Stroebel W, Ellwonger V, et al. Metastatic melanoma of unknown primary origin shows prognostic similarities to regional metastatic melanoma recommendations for initial staging examinations. Cancer. 1997;80(1):60-5.
18. Reintgen D.S., Cox C., Slingluff C.L., Jr., Seigler H.F. Recurrent malignant melanoma: the identification of prognostic factors to predict survival. Annals of Plastic Surgery. 1992;28:45–49
19. Tsilimparis N., Menenakos C., Rogalla P., Braumann C., Hartmann J. Malignant melanoma metastases as a cause of small bowel perforation. Onkologie. 2009;32:356–358
20. Amersi FF, Terando AM, Goto Y, et al: Activation of CCR9/CCL25 in Cutaneous melanoma mediates preferential metastasis to the small intestine. Clin Cancer Res 2008;14:638-645
21. Bender G.N., Maglinte D.D., McLarney J.H., Rex D., Kelvin F.M. Malignant melanoma:patterns of metastasis to the small bowel, reliability of imaging studies, andclinical relevance. American Journal of Gastroenterology. 2001;96:2392–2400.
22. Poggi S.H., Madison J.F., Hwu W.J., Bayar S., Salem R.R. Colonic melanoma, primary or regressed primary. Journal of Clinical Gastroenterology. 2000; 30:441–444.
23. Lens M., Bataille V., Krivokapic Z. Melanoma of the small intestine. Lancet Oncology. 2009;10:516–521
24. Balch CM, Soong SJ, Murad TM, Smith JW, Maddox WA, Durant JR. A multifactorial analysis of melanoma: IV: Prognostic factors in 200 melanoma patients with distant metastases: (Stage III) J ClinOncol. 1983;1:126–134.