Intravascular Papillary Endothelial Hyperplasia Mimicking Sister Mary Joseph Nodule in a Patient with Ovarian Carcinoma

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Abstract

Intravascular Papillary Endothelial Hyperplasia (IPEH) is a rare benign vascular lesion of the skin and subcutaneous tissues that results from the proliferation of endothelial cells within a blood vessel. In this article, we present the case of an IPEH mimicking a Sister Mary Joseph Nodule on the umbilicus of a 53-year old female patient with ovarian cancer. A diagnostic workup was performed with a computerized tomography of abdominal cavity and pelvis showing an expansive cystic tumor formation with probable ovarian origin. Two separate histopathologic readings were done on the cutaneous lesion which revealed contradicting findings of benign versus malignant tumors. Immunohistochemical stains done showed that the lesion was positive for ERG and negative for epithelial differentiation markers. No surgical intervention was done at the time of consultation as a cutaneous metastasis was primarily considered initially. It is crucial to rule out a diagnosis of Sister Mary Joseph nodule, especially in a background of ovarian carcinoma as it may mimic vascular lesions occurring on the umbilicus. Immunohistochemical staining is a significant tool to precisely diagnose such lesions so that it is neither inadequately nor aggressively managed.

Keywords: Intravascular Papillary Endothelial Hyperplasia, Masson's tumor, Sister Mary Joseph nodule, ovarian cancer, case report

INTRODUCTION

Intravascular Papillary Endothelial Hyperplasia (IPEH), also known as Masson's tumor or Masson's vegetant intravascular hemangioendothelioma (MVH) is a benign tumor that clinically presents as bluish to purplish red cystic masses containing sanguineous material. This case report describes an 53-year-old female diagnosed with an ovarian new growth presenting with umbilical skin lesions grossly resembling what was first thought of as a Sister Mary Joseph's (SMJ) nodule given the patient's background of a pre-existing carcinoma. It was upon further testing with immunohistochemistry that the final diagnosis was confirmed. Cutaneous metastasis like the SMJ nodule, although extremely rare is an important physical finding as it is a sign of advanced stage of malignancy. Hence, it was at the outset, considered in the case. However, it is also of significant to arrive with an accurate diagnosis in this case because it influences the management of the primary tumor and alleviates additional stress to the patient.

CASE REPORT

A 53-year old Filipino female patient presented with a 2-year history of slowly progressing abdominal enlargement with subsequent appearance of multiple, slightly tender papules and nodules on the umbilicus. The appearance of cutaneous lesions started 2 months prior to the referral of the Department of Obstetrics and Gynecology (OB-GYN) to the Department of Dermatology. Review of systems revealed accompanying significant weight loss and abdominal discomfort. The past medical and personal and social

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history were unremarkable. She had no history of previous surgeries. The family medical history revealed a history of diabetes mellitus in a sibling and myoma on the paternal side. On physical examination, the patient had evident ascites with a presence of skin-colored and hyperpigmented papules, few nodules and cystic mass on the umbilicus. Dermoscopy of the cutaneous lesions revealed patchy pseudo reticular network with thick brown lines surrounding a s tructureless area and a milky red structureless area some with white veil and multiple shiny white lines and strands (Figure 3). These dermoscopic features points out to a probable vascular lesion.

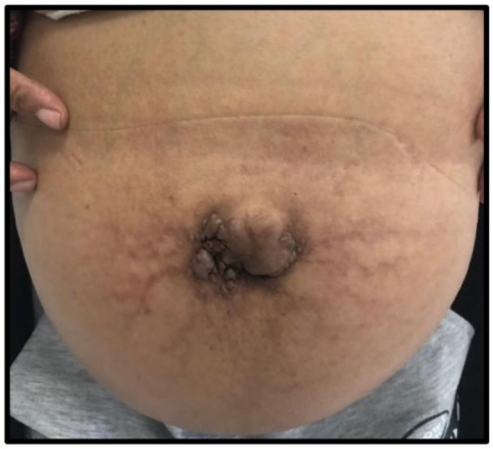

Figure 1. Abdomen distended and tense. Percussion reveals ascites with shifting dullness

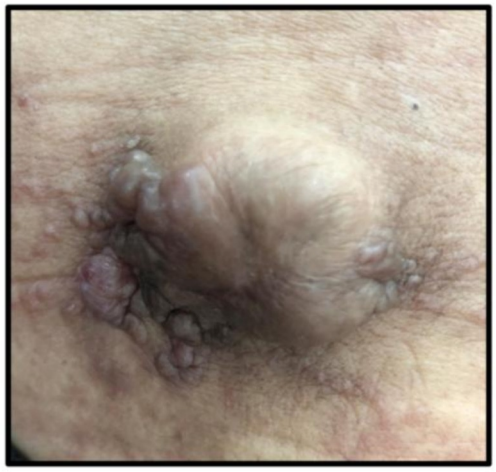

Figure 2. Multiple skin-colored to pinkish papules, few nodules and solitary cystic mass

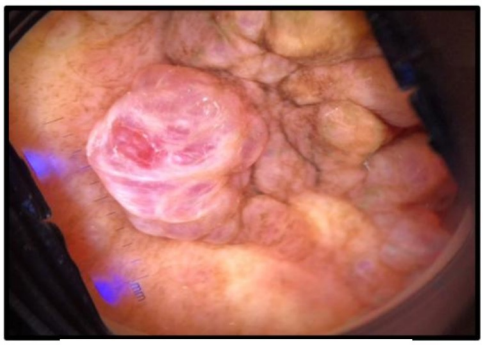

Figure 3. Dermoscopy of the lesion

Previous outpatient diagnostic workup done by the Department of OB-GYN revealed a normal sized anteverted uterus with thick endometrium suggestive of endometrial pathology and a pelvoabdominal mass probably an ovarian new growth with undetermined laterality, malignant by International Ovarian Tumor Analysis. A computerized tomography of the abdominal cavity and pelvis showed a huge complex mass, predominantly cystic, measuring 24.6 x 25.4 x 20.5 cm. Mass effect is seen displacing the surrounding structures peripherally. The uterus is unremarkable. The bowels are not dilated. Free fluid collection is seen in the peritoneal and pelvic cavities (Figure 4,5). Blood test demonstrated mild microcytic, hypochromic anemia, mild hyponatremia and hypocalcemia and increased levels of Cancer antigen 125 at >500 mg/dL. Chest radiograph showed pleural effusion on the bilateral lung. The Department of Dermatology did a 4 mm skin punch biopsy at 2 sites on the umbilicus. The histopathological result of skin biopsy revealed metastatic deposits of tumor cells over the dermis in an Indian file formation. Dilated lymph vessels and thinning of endothelial wall, containing atypical pleomorphic cells spill over the dermal interstitial fibers (Figure 6). These results were indicative of a cutaneous metastasis from a primary source. A separate reading was done by the Department of Pathology which revealed dilated vascular spaces lined by pleomorphic cells exhibiting mild atypia. Their primary consideration was intravascular papillary endothelial hyperplasia arising in a pre-existing lymphagioma or papillary hemangioma. Immunohistochemistry was performed paraffin-embedded tumor tissue. Tissue cells showed positive staining for ERG, which is a specific

immunohistochemical marker for vascular differentiation, including benign and malignant vascular tumors[1] (Figure 7). The cells of interest were negative for CK7, CK20, p63 and Pax8. Histomorphology and immunohistochemical profile supports the diagnosis of intravascular papillary endothelial hyperplasia.

Prior to performing the immunohistochemical staining, the patient was initially referred back to the OB-GYN Department with the apprising of a poor prognosis due to a consideration of a metastasis. Few days after her initial visit to Dermatology Department, patient noted recurrence of bleeding and was given first-aid management. The patient was then lost-to-follow-up due to the ongoing community quarantine in the area because of the COVID-19 pandemic. Until three months later, she was admitted by the primary service, co-managed by the Department of Internal Medicine, for management of worsening pleural effusion. Unfortunately, the patient was not optimized for further treatment of the primary tumor as a result of her deteriorating functional capacity. Meanwhile, the skin lesions have remained the same in size, without development of new lesions. Less than a week after admission, the patient expired due to pulmonary complications.

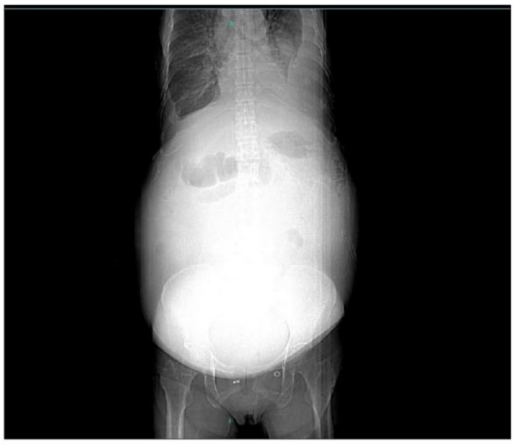

Figure 4. CT of abdominal cavity and pelvis showing an expansive tumor formation

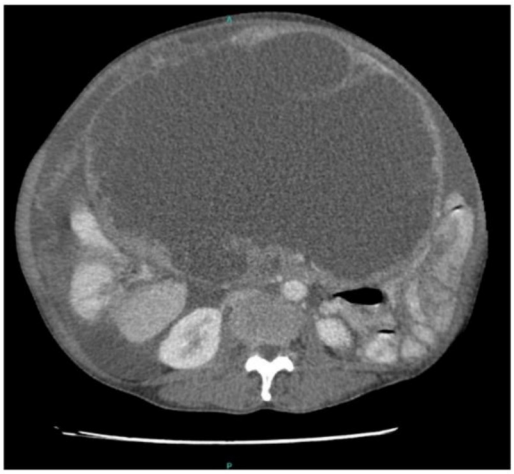

Figure 5. CT of abdominal cavity and pelvis with signs of tumor propagation to the front

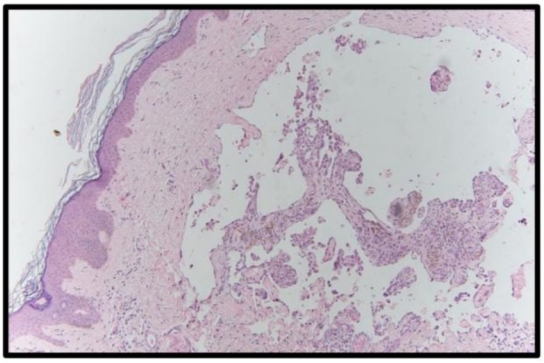

Figure 6. Histopathology showing dermal nests of neoplastic cells underneath intact epidermis (H&E, 40x)

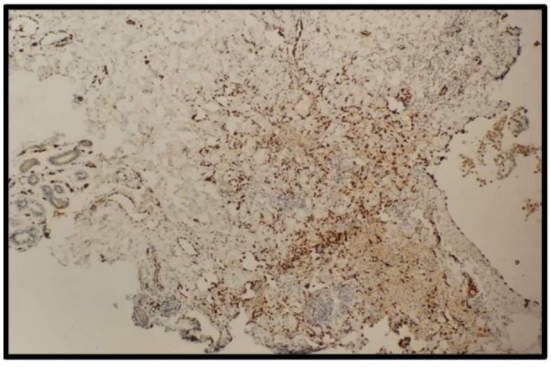

Figure 7. Immunohistostaining showing positivity for ERG in the cells of interest

DISCUSSION

Intravascular Papillary Endothelial Hyperplasia (IPEH), also known by its eponym Masson's tumor was first described by Pierre Masson in 1923 in an inflamed hemorrhoid of a 68-year old patient which he believed was a neoplastic lesion. He first called it Hémangioendothéliome végétant intravasculaire but later it was described as a reactive phenomenon by Henschen[3]. IPEH is a benign vascular lesion comprising around 2% of the vascular tumors of the skin and subcutaneous tissue. The condition is slightly predominant among females with a female to male ratio of 1.2:1[4]. It has a common incidence between the 3rd to 4th decade of life[5].

IPEH presents clinically as a sharply demarcated firm, bluish or purplish-red nodule or mass, measuring 0.5 to 5 cm, commonly seen on the fingers, trunk, head and neck. Based on the author's search, there were no previous reports yet of IPEH occurring on the umbilicus. Three variants have been described: (1) the primary form occurs within a dilated vessel, (2) the secondary or mixed form which occurs in association with a thrombus in the setting of a preexisting lesion, e.g. within a hemangioma, arteriovenous malformation, pyogenic granuloma, or varix and (3) the undermined type found in an extravascular location, in which the lesion develops in the bed of a hematoma and trauma is a prerequisite[2]. Our patient exhibits features of the second type.

The pathogenesis of IPEH is still poorly understood but literature review postulates a benign neoplastic process that involves proliferation of the endothelial cells in a papillary formation into the vascular lumen, which can be followed by obstruction and secondary degeneration. It typically follows a traumatic vascular stasis or thrombus. Basic fibroblast growth factor (FGF) appears to be released by the invading macrophages to the trauma site, initiating proliferation of endothelial cells[4] and activating a positive feedback loop of endothelial proliferation[5].

It is imperative to exclude several differential diagnoses of a patient presenting with an umbilical mass or nodule such as a primary umbilical neoplasm, cutaneous metastasis, umbilical hernia, umbilical endometriosis or epidermal inclusion cysts. In this patient, a diagnosis of cutaneous metastasis was originally considered because of the background of an ovarian carcinoma despite contradicting histopathologic findings on H&E stain. The definitive diagnosis of IPEH is obtained by tissue biopsy of the lesions and histologically, should be differentiated with hemangioma, pyogenic granuloma, and angiosarcoma. On tissue biopsy, the lesions of IPEH display dilated vessels that contains papillary proliferation of plump endothelial cells that are one to two cell thick[3]. It frequently overlies a fibrous tissue[6]. It lacks cellular atypia, although there are reported cases with moderate atypia[7]. Fibrin deposition and thrombi formation may be present without areas of necrosis[8].

Although seldom necessary, immunohistochemistry assists in arriving at the exact diagnosis. The cells of IPEH are differentiated endothelial cells, and thus, express markers such as vimentin, CD31, CD34, von Willebrand factor (vWF, factor VIII–related protein), factor XIIIa, and ULEX europaeus agglutinin (UEA-1)[3]. In our case, immunostaining has been instrumental to rule out the diagnosis of cutaneous metastasis and confirming the diagnosis of IPEH. Thus, the author strongly recommends that immunohistochemistry staining be done when the initial H&E findings are equivocal.

The treatment of IPEH requires complete surgical resection with or without wide margins of excision[9]. Sclerotherapy using sodium tetradecyl sulfate followed by surgery resulted in good aesthetic results and minimal intra-operative bleeding in a few reported cases. Recurrence of lesions is uncommon[3].

CONCLUSION

Sister Mary Joseph nodule, especially in a background of Ovarian carcinoma should still be considered as a valuable differential diagnosis as it may mimic vascular lesions occurring on the umbilicus. Although histopathology remains the gold standard in the diagnosis of intravascular papillary endothelial hyperplasia, immunohistochemical staining is vital to precisely diagnose this lesion so that it is neither

inadequately nor aggressively managed. It helps direct treatment options especially in patients with a consideration a cutaneous metastasis from a primary malignancy. It also crucial to prevent recurrence and morbidity.

Compliance with Ethical Standard

Conflict of interest. The authors declare that they have no conflict of interest.

Informed Consent. Informed consent was obtained from the patient and from her next of kin

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