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CASE REPORT

Primary anorectal malignant melanoma: A clinical, radiology and pathology correlation

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Abstract

*Introduction***:** Primary gastrointestinal melanomas are mucosal malignancies that arise from melanocytes in the oropharynx, rectum, and anus. Anorectal malignant melanoma (ARMM) are exceedingly rare, accounting for less than 1% of all melanomas, 0.1% of all rectal malignancies and 4% of anal malignancies. Diagnosis is frequently delayed as these lesions are often mistaken for haemorrhoids. Histological evaluation with special immunohistochemical stains is often necessary for definitive diagnosis. Due to the aggressive nature, 61% of patients with ARMM would already have lymph node involvement or distant metastases, by the time of diagnosis. Prognosis is usually poor with 5-year survival rate of <20%. We report a case of metastatic ARMM in an elderly lady who presented with symptoms and signs mimicking a haemorrhoid. *Case Report***:** A 69-year-old lady presented with one year history of intermittent rectal bleed and an anorectal mass that was initially treated as haemorrhoid. Colonoscopy showed a hyperpigmented mass in the anorectal region which was confirmed as malignant melanoma on histopathological examination. Imaging with CT and MRI demonstrated locally advanced tumour with distant metastases to the liver and lung. Patient was referred for palliative management. *Conclusion***:** ARMM is a rare malignancy and often presented with non-specific clinical signs. Diagnosis is frequently delayed without high index of suspicion. MRI pelvis is the imaging of choice to assess local extent of disease. Histologic evaluation with special immunohistochemical stains is often necessary for definitive diagnosis. Prognosis is poor despite surgical and chemotherapeutic interventions.

Keywords: Anorectal malignant melanoma, haemorrhoids, colonoscopy, MRI features, immunohistochemistry, S-100.

INTRODUCTION

Malignant melanoma can originate from either mucous membrane or cutaneous. Mucosal melanomas are rare malignancy with aggressive behaviour and have different biological and clinical presentations. Asian and darker-skinned individuals show a higher percentage of mucosal malignant melanoma compared to Caucasians.[1] The pathogenesis for the development of mucosal melanoma is still poorly understood. Among the primary mucosal malignant melanomas, anorectal region is the third most common site after the head and neck and the female genital tract.[1-3] Anorectal malignant melanoma (ARMM) comprises less than 1% of all melanomas, 0.1% of all rectal malignancies and 4% of anal malignancies.[2-4] There are no specific symptoms and clinical signs for ARMM thus it is extremely difficult to make the diagnosis base on clinical presentation alone. They have poor prognosis with 5-year survival rate <20%, in contrast to 80% for cutaneous melanoma.[4] We report a case of ARMM in an elderly lady who presented with intermittent rectal bleed and an anorectal mass that mimic a haemorrhoid.

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CASE REPORT

A 69-year-old lady with underlying systemic lupus erythematosus (SLE) on treatment, presented with intermittent painless per-rectal bleeding during defaecation for one year. She initially sought medical attention in a private center six months after having the symptoms and was diagnosed as hemorrhoids. Subsequently, she presented to our emergency department complaining of increasing frequency of per-rectal bleeding with mucous discharge, rectal pain and incontinence to gas and fluid of two months duration. There was no constitutional symptom. Her vital signs and laboratory markers were within normal limits.

Abdominal examination was unremarkable. Digital rectal examination revealed an irregular firm mass protruding from the posterior wall of anal verge, extending 6 cm proximally into the lower rectum. Proctoscopy showed a hyperpigmented mass at 6 o'clock position with contact bleeding. Abdominal and chest radiographs were unremarkable. Colonoscopy confirmed the presence of an ulcerated, polypoidal mass extending from the anal verge to 5cm from anal verge. The mass appears necrotic with contact bleeding (FIG. 1). Histopathological examination (HPE) of the mass revealed nests of heavily pigmented pleomorphic malignant cells containing melanin pigment, diagnostic of a malignant melanoma. This was confirmed with positive S-100, HMB-45 and CD117 immunohistochemical stains (FIG. 2).

In view of this diagnosis, a total body skin examination (TBSE) was performed to look for possible primary site. No cutaneous lesion was detected on screening TBSE. MRI pelvis showed a heterogenous enhancing polypoidal eccentric mass arising from the anal canal extending superiorly till the mid rectum from 3 to 9 o'clock position. This mass demonstrated hyperintensity on T1 weighted fat suppression (T1WFS) and hypointensity on T2 weighted (T2W). Diffusion restriction on diffusion weighted imaging (DWI) and apparent diffusion coefficient (ADC) were noted (FIG. 3). The rectal lumen was significantly narrowed; however, the proximal bowel was not dilated. This mass extends beyond the serosa layer and abuts the mesorectal fascia in the lower rectum. The right internal sphincter and puborectalis muscle were involved. Multiple metastatic regional lymph nodes were also observed (FIG. 4). Distant metastases to the regional lymph nodes, liver and lung were found

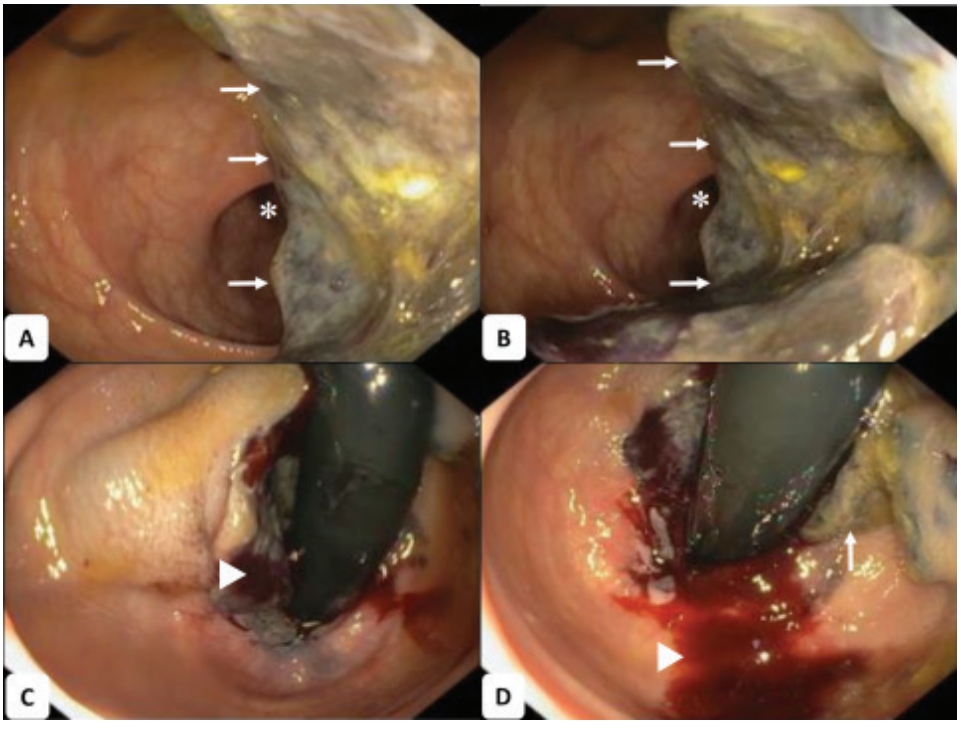

FIG. 1: Colonoscopy images (A and B) revealed ulcerated polypoidal mass (white arrow) causing luminal narrowing (asterix). Brownish surface pigmentation noted which appears necrotic. There are contact bleeding during colonoscopy (arrow head in image C and D).

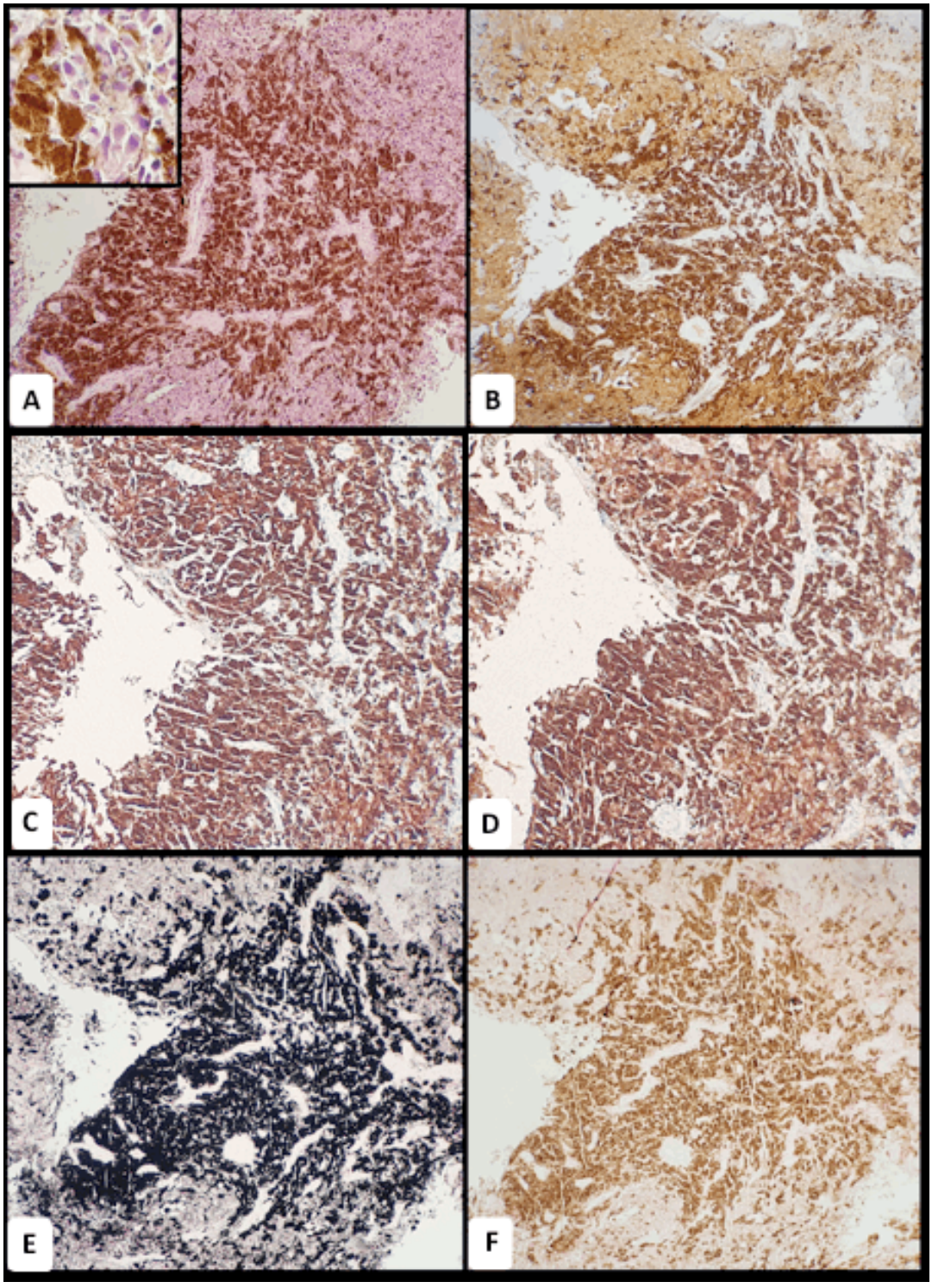

FIG. 2: (A) Microscopic image of the polypoid mass biopsy showing irregular nests and sheets of heavily pigmented cells within a fibrocollagenous stroma (H&E 10x). The inset shows coarse dark brown cytoplasmic pigments and polygonal cells with pleomorphic nuclei. These cells are positive for (B) S-100, (C) HMB-45 and (D) CD117. (E) The brown pigments stain black on Masson Fontana confirming the presence of melanin pigments and (F) remain unstained on Perl's Prussian Blue stain for iron.

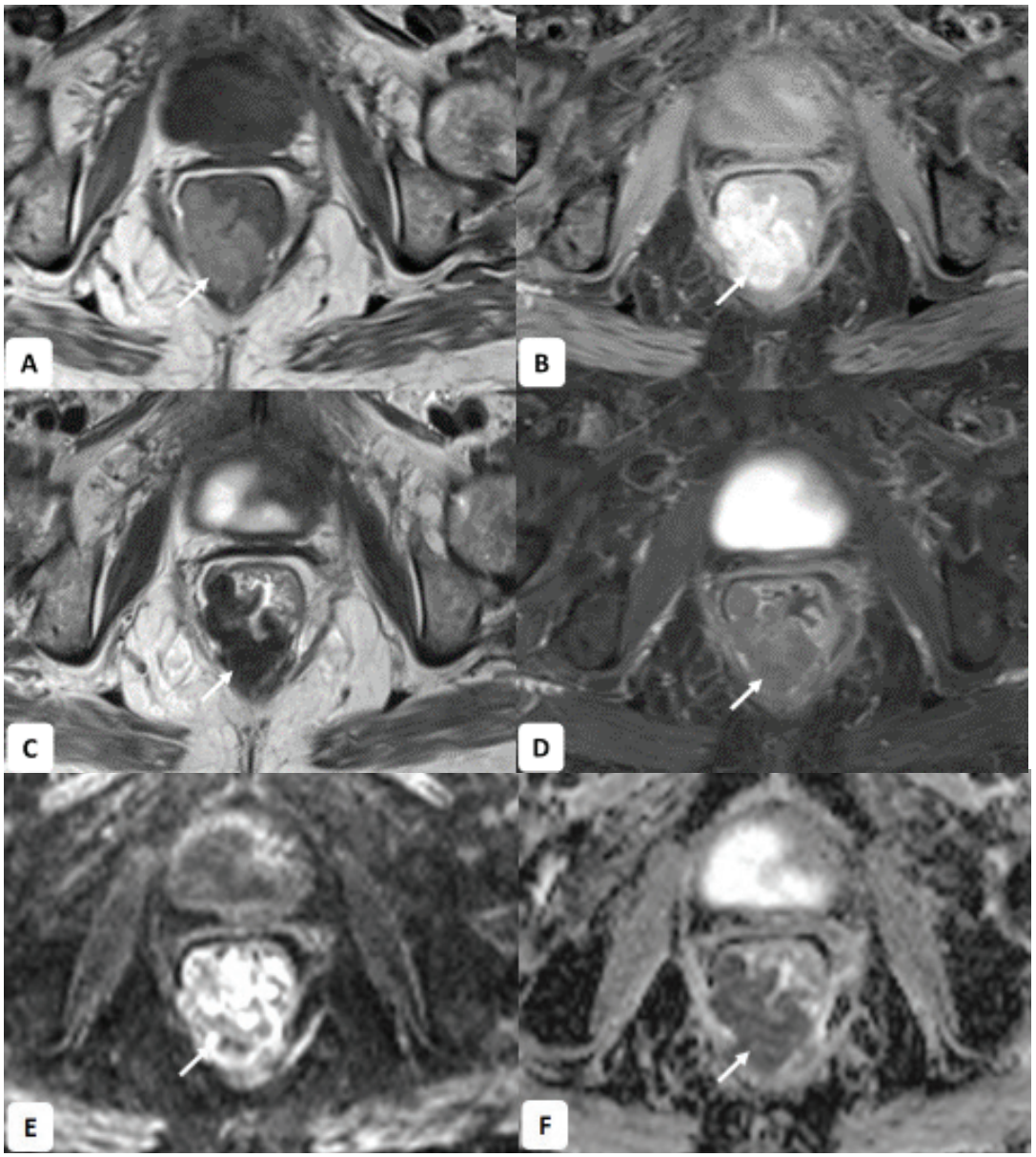

FIG. 3: MRI of the pelvis in axial T1W (A), T1WFS (B), T2W (C), post-contrast T1W (D), DWI at 800 b-value (E) and ADC (F) sequences highlighting bulky intraluminal polypoidal mass (white arrow) obscuring the lumen. The mass demonstrates T1W/T1WFS hyperintensity, T2W hypointensity, restricted diffusion in DWI/ADC and heterogenous enhancement on post-contrast.

on CT (FIG. 5).

In view of metastatic disease, the patient was referred for palliative management. She was offered laparoscopic assisted diverting sigmoid colostomy by surgical team; however, the patient was not keen for surgery. Immunotherapy was not started in view of her underlying autoimmune disease (SLE). Currently, the patient is still on palliative chemotherapy.

DISCUSSION

By definition, mucosal melanomas are malignant primary tumours originating from melanocytes located in the mucosal membranes. They have no direct association with the cutaneous melanoma as the postulation pathogenesis varies severely from cutaneous melanoma.[4] Cutaneous melanoma commonly associated with ultraviolet (UV) light[3,4,8] whereas pathogenesis of ARMM is still baffling and commonly being related to KIT

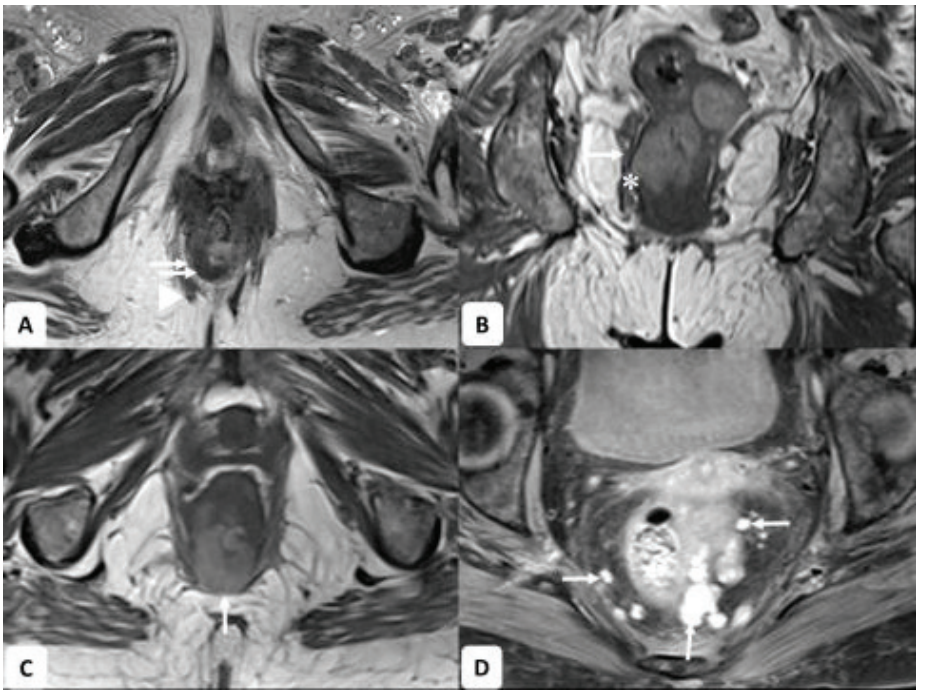

FIG. 4: MRI of the pelvis in axial T2W (A), coronal T1W (B),axial T1W (C) and axial T1WFS (D) demonstrating involvement of the right internal sphincter (white arrow in image A) with preservation of the external sphincter (arrow head in image A). There is involvement of the right puborectalis muscle (asterix in image B) and no clear fat plane with the right iliococcygeus muscle (white arrow in image B). The mass abuts the mesorectal fascia at lower rectum (white arrow in image C). Enlarged high signal intensity on T1WFS mesorectal and extra-mesorectal lymph nodes were observed (white arrow in image D), which

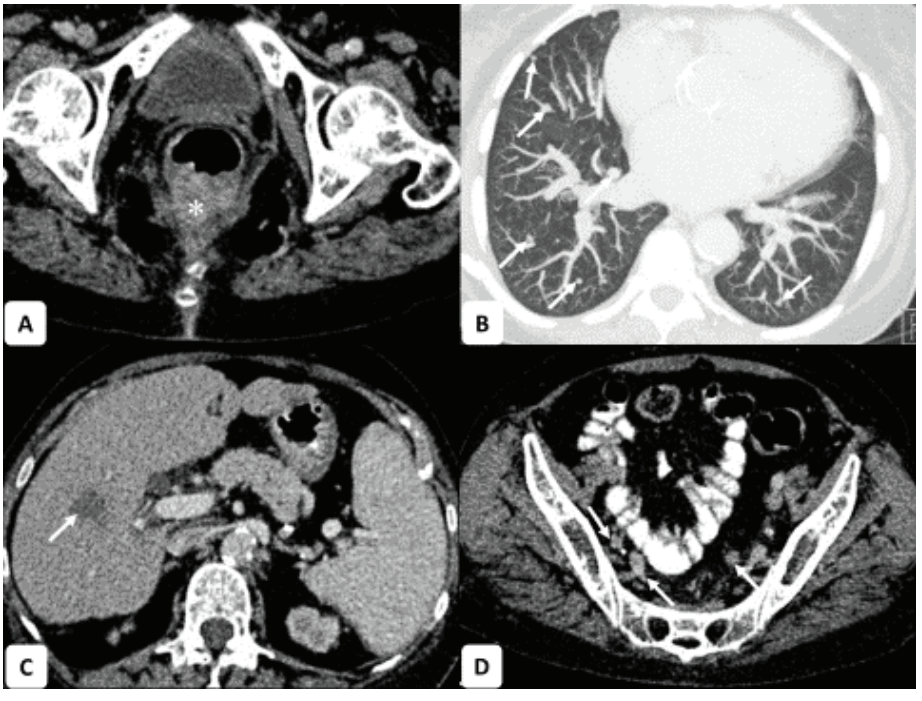

FIG. 5: CT-scan of thorax/abdomen/pelvis in axial cut showing heterogenous enhancing irregular bowel wall thickening involving the anorectum (asterix in image A). Images B, C and D revealed multiple lung (white arrow in image B), liver (white arrows in image C) and nodal (white arrow in image D) metastases.

mutation over BRAF and NRAS mutations.[1,4]

Primary anorectal malignant melanoma (ARMM) is a rare and aggressive malignancy, comprising of less than 1% of all melanomas, 0.1% of all rectal malignancies and 4% of anal malignancies.[2,4] Approximately, 20% of ARMM are amelanotic and endoscopically the lesion can resemble benign polypoidal tumour.[2,5] Furthermore, patients with ARMM do not exhibit any pathognomonic symptoms or clinical signs, thus in about two thirds of patients they are often misdiagnosed for other condition such as haemorrhoids, benign polyps and rectal cancer.[2,3,5,6,7] Therefore, in most cases they tend to present at a very late stage, commonly with metastatic disease.[1,2,5,8] The most common presenting symptoms are rectal bleeding, altered bowel habits, anal pain and anal pruritis, all of which were present in our patient.[2,4,5] Another common symptom is tenesmus which was not seen in this case.[2,4,6]

On colonoscopy, ARMM mostly arise in the proximal portion of the pecten and transitional zone around the dentate line although they can develop throughout the anus. They range from being small to bulky intraluminal polypoidal mass with or without ulceration that commonly associated with luminal narrowing. Despite this, these lesions hardly cause significant bowel obstruction.[2,3] In comparison, rectal adenocarcinoma commonly appears as infiltrative ulcerative mass that frequently narrows the lumen that leads to bowel obstruction.[2,3] Not all ARMM will manifest with visible surface pigmentation, making the diagnosis even more challenging.[3,6] In addition, a pigmented polypoidal anorectal mass can be easily mistaken as a thrombosed haemorrhoid.[2,3,6]

On imaging, as in other anorectal malignancies, pelvic MRI is the modality of choice and plays an important role in diagnosis and assessment of local extent of disease. It is a known fact that melanocytic component of melanomas has paramagnetic features where it shortens T1 relaxation time and increases T2 relaxation time. Thus, classically melanoma will appear hyperintense on T1W and hypointense on T2W images. However, not all ARMM, especially in cases of amelanocytic melanomas, will show these classical paramagnetic MRI characteristic causing differentiation from other anorectal diseases difficult based on signal intensity alone.[2,5] In a retrospective study of twelve cases with pathologically proven ARMM within 10-years duration by Park *et al*., majority of the lesions showed hyperintensity on T1W and high or mixed signal intensity on T2W images. All the lesions showed restricted diffusion and hyperenhancement post-contrast.[2] In a different retrospective study by Li *et al*. on 12 confirmed ARMM cases, 11 cases demonstrated hyperintensity on T1W and T1WFS showed better images for both ARMM and metastatic lesion.[8] However, the high signal in T1WFS cannot be distinguished from bleeding or concentrated secreting mucus. Thus, Li *et al*. suggested CT to differentiate these two characteristics.[8] CT is important to assess for distant metastases as these patients tend to present late due to delayed in diagnosis. Furthermore, ARMM and metastatic lesions will demonstrates high metabolic activity in PET-CT making it recommended for staging and respond assessment.[5]

Histopathological examination (HPE) is still a pre-requisite and gold-standard for diagnosis of ARMM because not every case will show the typical paramagnetic features of melanin on imaging. Morphologically, the tumour cells vary considerably in size and shape. Most commonly, they have an epithelioid appearance with large hyperchromatic irregular nuclei. Multinucleation and bizarre giant cells are common in contrast to adenocarcinoma and squamous cell carcinoma. When present, brown pigments are fine and densely distributed in the cytoplasm. Less commonly, the tumour cells may be small and round resembling lymphocytes, spindle shaped resembling a sarcoma or arrayed in a trabecular fashion resembling a carcinoid.

Most literature suggested that immuno-histochemistry analysis is compulsory to distinguish ARMM from other malignancies, whereby a positive staining for S-100 is sensitive and HMB-45 is specific for malignant melanoma.[2-6,8] Other markers that are available include Melan A and vimentin. These immunohistochemistry markers will be intensely positive in 78-100% of ARMM.[4] In our case, the biopsied specimen has the classical epithelioid appearance with positive S-100 and HMB-45 staining.

Molecular studies have shown that the mitogen-activated protein kinase (MAPK) pathway is triggered notably by KIT, BRAF and NRAS mutations with up to 35.5% of ARMMs harbouring kit mutations.[9] The immunohistochemical stain CD117 (c-KIT) is used as a surrogate marker to detect the presence of KIT mutations. However, there is poor correlation between CD117 positive tumours

with KIT gene mutation and molecular testing is advised if there are plans for targeted treatment such as with imatinib.

The prognosis for these patients is usually poor with a 5-year survival rate of only less than 20%[2-6] and a median survival range of only 12-24months.[1,3,7] Individuals with a large tumour at presentation, metastatic disease or rapid relapse after initial treatment have poorer outcome. These were proven in a retrospective study by Heptt *et al*. in 444 patients diagnosed with mucosal melanoma within 27-years duration in their centre, 97 patients of ARMM had more advanced nodal status, higher percentage of metastatic disease at the time of diagnosis and poor overall survival rate.[1] The poor prognosis may be attributable to the fact that delayed diagnosis lead to advance and nonresectable disease at the time of diagnosis. Although various treatment modalities for ARMM have been suggested including surgical resection such as abdominoperineal resection and wide local excision, chemotherapy, and radiotherapy, all of them are debatable and there is a lack of evidence due to its rarity.[3,5-8] New targeted therapies and immunotherapies are still under investigation for patients with both metastatic and primitive melanoma.[5,7] Palliative surgery (such as local segmental resection or a diverting colostomy for bowel obstruction) is suggested in large primary tumours or in the presence of distant metastases.[5] Our patient has to undergo palliative therapy and she is not suitable for immunotherapy because of underlying SLE.

CONCLUSION

Primary anorectal malignant melanoma is a rare and aggressive malignancy. Awareness of this malignancy is important because of the lack of early specific signs and the patients with the symptoms were often mistakenly treated as benign disease. Hence, high index of clinical suspicion is necessary especially among the at risk age group. MRI is the most efficient diagnostic tool for this rare malignancy together with HPE confirmation. Although surgery is feasible and various target therapy is available, the overall prognosis remains unfavourable.

Authors' contribution: Literature search and original draft of the manuscript were prepared by SB. The clinical, radiological and pathological input were contributed by PKS, MTRH, CWY and CTK respectively. The manuscript was edited by PKS, MTRH, CWY and CTK. All authors approved the final version of the manuscript and take responsibility for the statements in the article.

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