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Original Article

Radiology Section

Magnetic Resonance Imaging findings in Primary Extracutaneous Melanoma from a Tertiary Cancer Care Centre: A Retrospective Cohort Study

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ABSTRACT

Introduction: Extracutaneous melanomas are rare, aggressive type of tumour, clinically and biologically distinct from their cutaneous counterpart. The two large broad categories of the extracutaneous melanomas are ocular and mucosal subtypes. Melanomas are classically hyperintense on T1 weighted images and hypointense on T2 weighted images due to the paramagnetic effects of melanin and presence of paramagnetic elements.

Aim: To describe the Magnetic Resonance Imaging (MRI) findings in primary extracutaneous melanomas at various anatomic sites.

Materials and Methods: This was a retrospective cohort study in which 13 cases of primary extracutaneous melanomas were identified from Picture Archiving and Communication System (PACS) archive over a period of eight years (January 2013-December 2020). Location and morphology of the tumour, signal intensity characteristics in T1 weighted, T2 weighted (hyperintense/isointense/hypointense to adjacent muscle) and Diffusion Weighted Imaging (DWI) (presence or absence of diffusion restriction) were analysed.

Results: The ocular melanomas (n=2) were seen as well-defined small intraocular mass attached to the choroid. The mucosal melanomas of the nasal cavity (n=2), rectum (n=4), vagina (n=3) and cervix (n=2) presented as large intraluminal polypoidal masses. Three categories of MRI appearances emerged in this study. Majority of the cases (n=8) showed hyperintense signals in T1-weighted images and hypointense signals in T2 weighted images (category 1). Diffusion restriction was seen in all cases (n=13) with low Apparent Diffusion Coefficient (ADC) values which ranged from 439-966 mm/sec with an average value of 755 mm/sec.

Conclusion: T1 and T2 shortening are typical of melanoma, the absence of these does not exclude the diagnosis. Although diffusion restriction and low ADC values help in the diagnosis of these tumours, they do not tend to play a specific role in the diagnosis.

Keywords: Apparent diffusion coefficient, Diffusion weighted imaging, T1 and T2 weighted imaging

INTRODUCTION

Malignant melanoma develops from melanocytes derived from neural crest cells. They usually occur in the skin (cutaneous melanoma), but they can also occur in any organ with melanin containing cells. Only 4-5% of primary melanomas are extracutaneous of which 70% are ocular and remaining are the mucosal subtype [1,2]. Extracutaneous melanomas are rare, aggressive type of tumour clinically and biologically distinct from the cutaneous counterpart. The two large broad categories of the extracutaneous melanomas are ocular and mucosal subtypes. Ocular melanoma is the most common primary eye tumour in adults and second most common type of melanoma after cutaneous subtype [2]. Mucosal melanoma arises from different mucosal lined organs; which include sinonasal tract, oral cavity, gastrointestinal tract (oesophagus, anorectum and biliary) and genito-urinary tract (vulva, vagina, cervix and urethra). Mucosal melanomas tend to occur in elderly patients with a median age at diagnosis of 70 years, having no clear predisposing factors and more prevalent in females; possibly due to increased incidence of vulvovaginal melanoma. They are diagnosed late and associated with poor outcome with an overall survival rate of 25% compared to 81% with cutaneous melanoma [3,4].

Extracutaneous melanomas tend to metastasise to various organs like lymph node, bone, lung, liver, spleen, gastrointestinal tract and subcutaneous tissue [4]. Melanomas are classically hyperintense on T1 weighted images and hypointense on T2 weighted images due to the paramagnetic effects of melanin and presence of paramagnetic elements, including copper, manganese and zinc [5-7]. Diffusion restriction with low ADC values have also been described. The purpose of this study was to describe the imaging findings in primary extracutaneous melanomas at various anatomic sites and look for any specific finding in MRI which would be helpful for its diagnosis by retrospectively evaluating the imaging archives of institution.

MATERIALS AND METHODS

This retrospective cohort study was conducted in the Department of Radiodiagnosis, affiliated to a tertiary cancer centre in Southern India (Regional Cancer Centre, Thiruvananthapuram, Kerala, India). MRI scans done between January 2013-December 2020 were retrieved from PACS. Institutional Review Board (IRB) approval was obtained for this study (IRB no 07/2021/04). Written consent was waived. Data collection and analysis was done over a period of one month after obtaining IRB clearance. A total of 1400 melanomas (cutaneous and extracutaneous) were reported from this tertiary cancer care centre during the study period, mostly of cutaneous origin. Authors retrospectively identified cases from PACS system (GE centricity) to select subjects for this study. Out of the 78 cases of primary extracutaneous melanomas, 13 cases diagnosed with primary extracutaneous melanoma in this centre were identified for this study.

Inclusion criteria: Patients with primary extracutaneous melanoma who had initial MRI workup done at this centre with histological proven cases were included in the study.

Exclusion criteria: The patients who had their initial imaging done elsewhere or who had technically poor quality scans were excluded (n=65).

Imaging

The MRI was performed on 1.5 Tesla machine (GE Health care Milwaukee WI). In MRI the following features were analysed: tumour location, shape, signal intensity characteristics, and ADC value on DWI sequences. In addition other features like infiltration of surrounding tissues and lymphadenopathy were also noted. Each MRI examination was evaluated by two radiologists to determine the signal intensity of the lesion on T1-weighted and T2-weighted imaging when compared with adjacent musculature and categorised as hypointense/isointense/hyperintense signals relative to muscle in each sequence. Cases which showed hyperintense signals on T1-weighted images and hypointense signals on T2 weighted images (category 1). Cases which showed hypointense signals on T1-weighted images and hyperintense signal on T2 weighted images (category 2). Cases which showed hyperintense signals on both T1 and T2 weighted images (category 3).

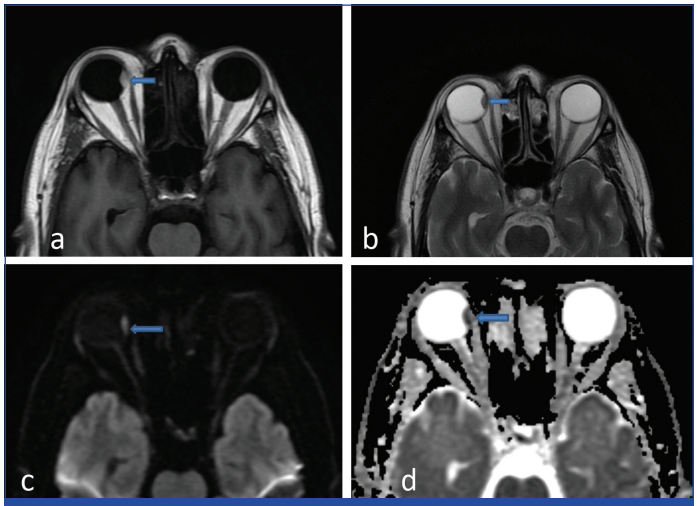
STATISTICAL ANALYSIS

Descriptive statistics with analysis of frequency and percentage of various parameters was done.

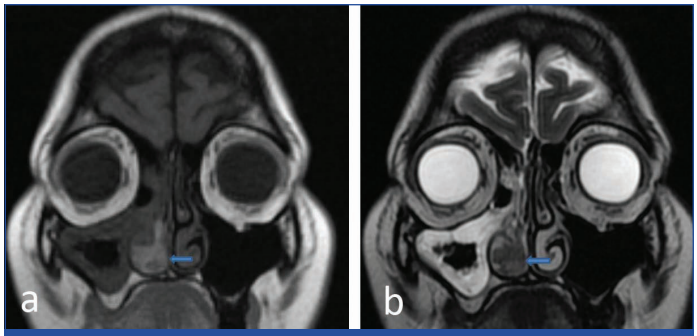
RESULTS

The age of presentation in this study cohort ranged from 33-80 years with a mean age of 62±10 years. This study population showed a slight female preponderance, seven females and six males, possibly due to inclusion of female genital tract melanomas. Primary location of the tumour were in the choroid (n=2), nasal cavity (n=2) rectum (n=4), vagina (n=3) and cervix (n=2).

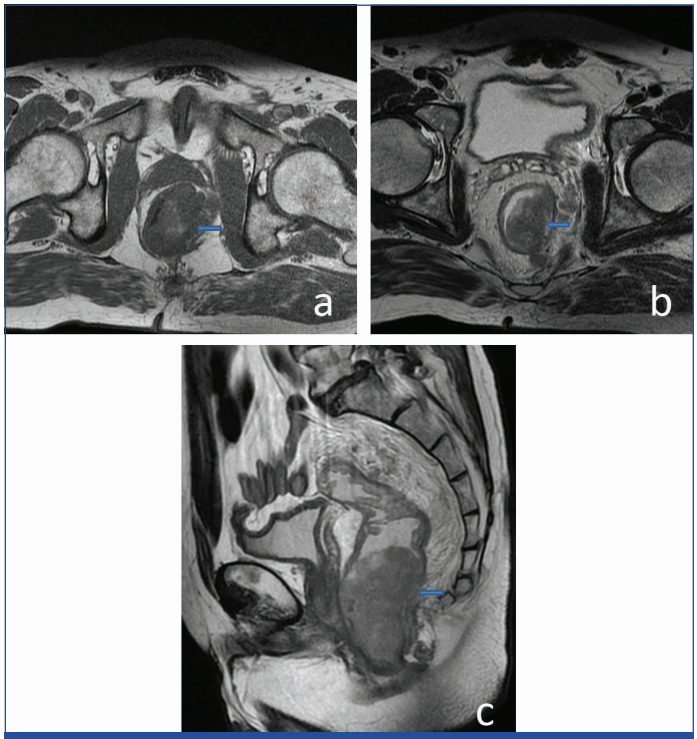
Tumour location and morphology: The ocular lesions were seen as well-defined small intraocular mass attached to the choroid. No extraocular extension was seen [Table/Fig-1a-d]. Nasal mucosal melanomas were seen as polypoid mass arising from the lateral nasal wall [Table/Fig-2a,b]. Bone destruction and lymph node enlargement were seen in one patient. Rectal melanomas were seen as large polypoid non obstructing intraluminal masses [Table/Fig-3a-c]. Perirectal infiltration was seen in one patient and lymphadenopathy in three patients [Table/Fig-3a,b], [Table/Fig-4a-d]. Out of the three patients with vaginal melanoma, only one showed infiltration into the surrounding fat, remaining two were confined to vaginal wall with intraluminal component [Table/Fig-5 a-d]. Melanoma of cervix were also seen as large intraluminal polypoid mass [Table/Fig-6a,b] and



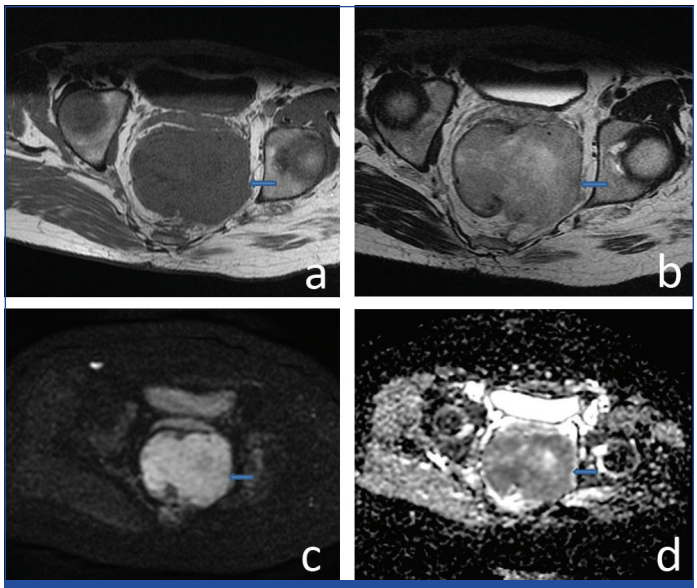
[Table/Fig-1]: a) Axial T1 weighted images MRI of orbit shows intraocular lesion in right eye (blue arrow) showing hyperintense signals; b) Axial T2 weighted MR images of orbit shows lesion (blue arrow) to be hypointense to vitreous; c-d) Axial DWI and ADC map of intraocular mass (blue arrow), showing hyper intense signals in DWI and hypointense signal in ADC. (Images from left to right)



[Table/Fig-2]: a) Coronal T1 weighted images shows hyperintense signal lesion arising from lateral wall of right nasal cavity (blue arrow); b) Coronal T2 weighted images shows hypointense mass within the right nasal cavity (blue arrow). (Images from left to right)

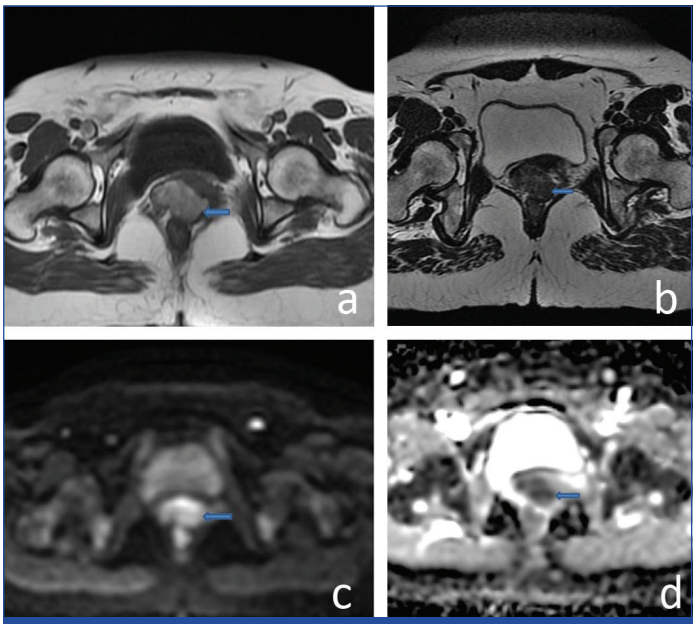


[Table/Fig-3]: a) Axial T1 weighed MR images of rectum shows an intraluminal polypoid mass (blue arrow) in in distal rectum. Hyperintense signal areas are present within the mass; b) Axial T2 weighted images shows the mass in distal rectum (blue arrow) is predominantly hypointense; c) Sagittal T2 weighted images shows non obstructing intra luminal polypoid mass (blue arrow) in distal rectum and anal canal. (Images from left to right)

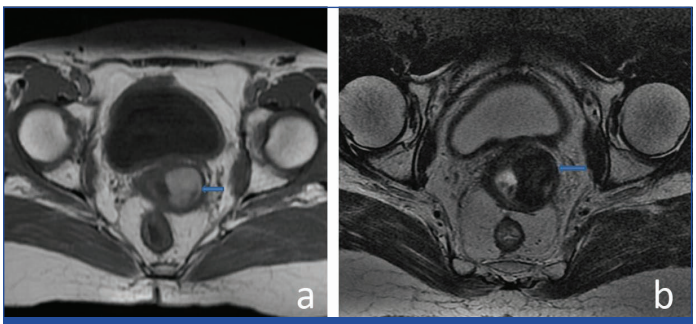


[Table/Fig-4]: a-b) Axial T1 weighted images show hypointense signal mass (block arrow) in rectal lumen with perirectal infiltration. Axial T2 weighted shows hyperintense signal of the mass (blue arrow); c-d) Axial DWI shows hyperintense signals in rectal mass (block arrow). Axial ADC map shows hypointense signal in mass (blue arrow). (Images from left to right)

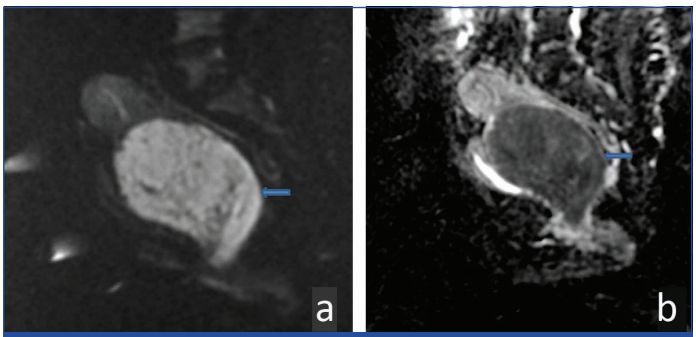
[Table/Fig-7a,b]. Neither parametrial infiltration nor lymphadenopathy was seen any of the cases with melanoma of cervix.



[Table/Fig-5]: a) Axial T1 weighted images of pelvis intravaginal mass (blue arrow) with hyper intense signals; b) Axial T2 weighted images show hypointense signals in vaginal mass (blue arrow); c-d) Axial DWI shows hyperintense signals in vaginal mass (blue arrow). Axial ADC map shows hypointense signal within the mass (blue arrow). (Images from left to right)



[Table/Fig-6]: a) Axial T1 weighted images shows mass lesion in left lateral wall of cervix with hyperintense signals (blue arrow); b) Axial T2 weighted images show hypointense signals in mass in cervical canal (blue arrows). (Images from left to right)



[Table/Fig-7]: a-b) Coronal DWI and ADC map shows a large mass (blue arrow) in endocervical canal with diffusion restriction. (Images from left to right)

Imaging findings: Three categories of MRI appearances were demonstrated in this study. Majority of the cases (n=8) showed hyperintense signals on T1-weighted images and hypointense signals on T2 weighted images (category 1). Four cases showed hypointense signals on T1-weighted images and hyperintense signal on T2 weighted images (category 2).The remaining one case showed hyperintense signals on both T1 and T2 weighted images (category 3). Diffusion restriction was seen in all cases with low ADC values which ranged from 439-966 mm/sec with an average value of 755±201 mm/sec. The MRI signal characteristics of each lesion in various anatomical location is given in [Table/Fig-8].

Anatomical site	T1WI	T2WI	DWI	ADC (value)
Ocular (n=2)	hyperintense	hypointense	hyperintense	low (895)
	hyperintense	hypointense	hyperintense	low (885)
Nasal cavity (n=2)	hyperintense	hypointense	hyperintense	low (802)
	hyperintense	hypointense	hyperintense	low (758)
Rectum (n=4)	hyperintense	hypointense	hyperintense	low (847)
	hypointense	hyperintense	hyperintense	low (617)
	hypointense	hyperintense	hyperintense	low (966)
	hypointense	hyperintense	hyperintense	low (439)
Vagina (n=3)	hyperintense	hypointense	hyperintense	low (777)
	hyperintense	hypointense	hyperintense	low (764)
	hypointense	hyperintense	hyperintense	low (545)
Cervix (n=2)	hyperintense	hypointense	hyperintense	low (746)
	hyperintense	hyperintense	hyperintense	low (771)

[Table/Fig-8]: MRI characteristics of study group (13 cases).

DISCUSSION

Extracutaneous melanomas are rare tumours with poor prognosis. The incidence of extracutaneous melanoma in this study in comparison to other studies is mentioned in [Table/Fig-9] [1,8-11]. Accurate diagnosis of this disease is required to prevent early metastatic spread [2]. Treatment modalities usually are surgery, radiotherapy, chemotherapy and immunotherapy depending on the primary site of tumour and metastatic disease. According to various literature reviewed ocular subtype is the most common primary extracutaneous melanoma [2,5]. In this study, only two cases of ocular melanoma was observed. The other patients treated in this institution were those who were diagnosed and investigated at other ophthalmology centres and referred to us for treatment; hence were not included in this study. The median age at the time of diagnosis of non cutaneous melanoma was 56 years in this study which was similar to recent study by Lian B et al., which included 706 patients. In this study, there is slight female preponderance (54%) compared to male (46%) which was similar to that in literature, primarily because melanoma arising within the female genital tract is more common [2-4] .

Study	Incidence of ECM (%)
Mc Laughlin CC et al., 2005 [1]	5.10%
Scotto J et al., 1976 [8]	14.00%
Chang AE et al.,1998 [9]	8.80%
Koomen ER et al., 2010 [10]	6.90%
Singh SRK et al., 2021 [11]	6%
Current study	5.60%

[Table/Fig-9]: Comparison of incidence of extracutaneous melanomas in various studies [1,8-11].

Traditionally melanomas tend to shorten T1 and T2 relaxation time due to its paramagnetic effect, resulting in hyperintense signals on T1 weighted imaging and hypointense signals on T2 weighted imaging [5-7]. Signal intensities can be correlated with percentage of melanin containing cells in tumour; greater the concentration of melanin, greater the high signal intensity on T1 weighted images [7,12]. In the current study majority of the cases (62%) showed typical appearance of melanoma. A total of 31% of the cases showed signal intensity shown by other tumours, i.e. hypointense signals on T1 weighted imaging and hyperintense signals on T2 weighted imaging and remaining appeared hyperintense in both T1 and T2 weighted sequences. The study by Marx HF et al., describing the MRI features in melanoma also showed similar signal intensity patterns [6]. Their study proposed various explanations for the other spectrum of imaging findings other than the classical one such as differing concentrations of melanin, propensity for hemorrhage, use of wide range of Repetition Time (TR) and Time to Echo (TE)

values and signal intensity of surrounding tissue (as in the case of choroid melanoma where the background vitreous humour will help to enhance the signal of the tumour).

Morphology of the tumour and MR signal characteristics of melanomas at various anatomical sites in this study are as follows:

Ocular: According to literature [5,12], ocular melanoma most commonly occurs in uvea of which choroid melanoma is most common subtype. In the two cases of ocular melanoma in this study, mass was seen arising from the choroid lining. Both lesions appeared hyperintense on T1-weighted images hypointense on T2-weighted images. Case studies by Houle V et al., and Jiblawi A et al., on choroidal melanoma also showed similar MRI signal pattern [13,14].

Nasal cavity: In this study, frequent site of origin of nasal cavity melanoma was lateral nasal wall (83%). Literature review showed that majority of the lesions rise in the lateral nasal wall and nasal septum followed by maxillary sinus [3,15]. Both the lesions in this study appeared hyperintense on T1-weighted images and hypointense on T2-weighted images. In a study of MRI findings in sinonasal melanoma on 12 patients by Yousem DM et al., 60% patients showed T1 hyperintensity [16]. Signals on T2WI was variable in the study appearing hypo, iso or hypointense.

Rectum: All patients with rectal melanoma had presented with intraluminal large polypoid mass with focal luminal expansion and without bowel obstruction. This observation was similar to study done by Park HJ et al., evaluating the MRI findings of anorectal melanoma in 12 patients in which similar morphology was seen in all cases [17]. In the present study, 25% cases of rectal melanomas showed hyperintense signals on T1-weighted images and hypointense on T2-weighted images as expected; remaining 75% cases showed hypointense signals on T1-weighted images and hyperintense on T2-weighted images. In the study by Park HJ et al., [17] T1 hyperintensity was seen in about 66% and 33% had iso intense signals, contrary to this study. Their study showed perirectal infiltration in all patients (100%) and lymph node enlargement in 75%; Perirectal infiltration and lymphadenopathy was seen in 75% of patients in current study. Diffusion restriction was seen in all their cases, similar to this study.

Vagina: Vaginal melanomas appeared as intraluminal polypoidal masses in this study. One of the patients showed infiltration of parametrial fat while other two remained confined to vaginal wall. Lymph node enlargement was not seen in any. In this study lesions appeared hyperintense in T1 weighted images and hypointense in T2 weighted images in 66%. In the study done by Takehara M et al., [18] in six patients with melanoma of female genital tract, 75% patients with vaginal melanoma had high signal intensity on T1-weighted images similar to this study. In case studies by Moon WK et al. and Kim H et al., [20] it was concluded that if the vaginal mass showed intermediate to high signal intensity on T1 weighted images, melanoma should be considered [19,20].

Cervix: Melanoma of cervix in this study were seen as large polypoid lesions in the endocervical canal without invasion of stroma. Parametrial infiltration or lymphadenopathy was not seen. Both lesions showed hyperintense signals on T1-weighted images. But on T2 weighted images one lesion appeared hypointense as expected while the other appeared hyper intense. Only very few case reports have been published regarding melanoma of cervix. A case report by Lee JH et al., showed hyperintense mass in T1 weighted images with parametrial infiltration and bone metastasis [21]. The study by Takehara M et al., also included a case with mass in cervix which had a high signal intensity on both T1 and T2-weighted images [18].

ADC: The ADC values were evaluated for all the 13 patients who underwent MRI evaluation. The values are as mentioned in [Table/Fig-8]. The ADC values ranged from 439-966 mm/sec with an average value of 755 mm/sec. In the study by Erb-Eigner K et al., on 44 patient with ocular melanoma, it was found that melanomas tend to show low ADC value below 1000 mm/sec with a mean ADC value of 891 mm/sec [22]. In the study by Liu QY et al., on patients with vaginal melanoma an average ADC value of 647 mm/sec was obtained [23]. The ADC values obtained in this study was comparable to the values obtained in the above two studies.

Limitation(s)

Due to rareness of this disease entity only a small sample size could be included. As MRI findings were only analysed, this study had to exclude patients with buccal mucosal melanoma for which imaging modality used is Computed Tomography (CT) scan.

CONCLUSION(S)

Melanomas become the most important differential in a large polypoidal intraluminal non obstructing mass with high signal intensity on T1 weighted images and low signal intensity on T2 weighted images in MR imaging in a mucosa lined organ. Signal patterns showing T1 and T2 shortening are typical of melanoma, the absence of these does not exclude the diagnosis. Although diffusion restriction and low ADC values help in the diagnosis of these tumors, they do not tend to play a specific role in the diagnosis. Because of rarity of this entity a multi-institutional study will be more useful for better understanding.

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REFERENCES

[1] McLaughlin CC, Wu XC, Jemal A, Martin HJ, Roche LM, Chen VW. Incidence of noncutaneous melanomas in the U.S. Cancer. 2005;103(5):1000-07.
[2] Keraliya AR, Krajewski KM, Braschi-Amirfarzan M, Tirumani SH, Shinagare AB, Jagannathan JP, et al. Extracutaneous melanomas: A primer for the radiologist. Insights Imaging. 2015;6(6):707-17.
[3] Carvajal RD, Spencer SA, Lydiatt W. Mucosal melanoma: A clinically and biologically unique disease entity. J Natl Compr Canc Netw. 2012;10(3):345-56.
[4] Lian B, Cui CL, Zhou L, Song X, Zhang XS, Wu D, et al. The natural history and patterns of metastases from mucosal melanoma: An analysis of 706 prospectively-followed patients. Ann Oncol. 2017;28(4):868-73.
[5] Wong VK, Lubner MG, Menias CO, Mellnick VM, Kennedy TA, Bhalla S, et al. Clinical and imaging features of noncutaneous melanoma. AJR Am J Roentgenol. 2017;208(5):942-59.
[6] Marx HF, Colletti PM, Raval JK, Boswell WD Jr, Zee CS. Magnetic resonance imaging features in melanoma. Magn Reson Imaging. 1990;8(3):223-29.
[7] Premkumar A, Marincola F, Taubenberger J, Chow C, Venzon D, Schwartzentruber D. Metastatic melanoma: Correlation of MRI characteristics and histopathology. J Magn Reson Imaging. 1996;6(1):190-94.
[8] Scotto J, Fraumeni JF Jr, Lee JA. Melanomas of the eye and other noncutaneous sites: Epidemiologic aspects. Journal of the National Cancer Institute. 1976;56(3):489-91.
[9] Chang AE, Karnell LH, Menck HR. The National Cancer Data Base report on cutaneous and noncutaneous melanoma: A summary of 84,836 cases from the past decade. The American College of Surgeons Commission on Cancer and the American Cancer Society. Cancer. 1998;83(8):1664-78.
[10] Koomen ER, de Vries E, van Kempen LC, van Akkooi AC, Guchelaar HJ, Louwman MW, et al. Epidemiology of extracutaneous melanoma in the Netherlands. Cancer Epidemiol Biomarkers Prev. 2010;19(6):1453-59.
[11] Singh SRK, Malapati SJ, Kumar R, Willner C, Wang D. NCDB Analysis of Melanoma 2004-2015: Epidemiology and Outcomes by Subtype, Sociodemographic Factors Impacting Clinical Presentation, and Real-World Survival Benefit of Immunotherapy Approval. Cancers (Basel). 2021;13(6):1455.
[12] Isiklar I, Leeds NE, Fuller GN, Kumar AJ. Intracranial metastatic melanoma: Correlation between MR imaging characteristics and melanin content. AJR Am J Roentgenol. 1995;165(6):1503-12.
[13] Houle V, Bélair M, Allaire GS. AIRP best cases in radiologic-pathologic correlation: choroidal melanoma. Radiographics. 2011;31(5):1231-36.
[14] Jiblawi A, Chanbthis H, Tayba A, Khayat H, Jiblawi K. Magnetic resonance imaging diagnosis of choroidal melanoma. Cureus. 2021;13(7):e16628.
[15] Clifton N, Harrison L, Bradley PJ, Jones NS. Malignant melanoma of nasal cavity and paranasal sinuses: Report of 24 patients and literature review. J Laryngol Otol. 2011;125(5):479-85.
[16] Yousem DM, Li C, Montone KT, Montgomery L, Loevner LA, Rao V, et al. Primary malignant melanoma of the sinonasal cavity: MR imaging evaluation. Radiographics. 1996;16(5):1101-10.
[17] Park HJ, Kim HJ, Park SH, Lee JS, Kim AY, Kim SW, et al. JTHISNAL CLUB: Primary anorectal melanoma: MRI findings and clinicopathologic correlations. AJR Am J Roentgenol. 2018;211(2):W98-108.

[18] Takehara M, Saito T, Mizumoto H, Baba T, Tanaka R, Fujimoto T, et al. Imaging studies in patients with malignant melanoma in the female genital tract. Int J Gynecol Cancer. 2002;12(5):506-09.
[19] Moon WK, Kim SH, Han MC. MR findings of malignant melanoma of the vagina. Clin Radiol. 1993;48(5):326-28.
[20] Kim H, Jung SE, Lee EH, Kang SW. Case report: Magnetic resonance imaging of vaginal malignant melanoma. J Comput Assist Tomogr. 2003;27(3):357-60.
[21] Lee JH, Yun J, Seo JW, Bae GE, Lee JW, Kim SW. Primary malignant melanoma of cervix and vagina. Obstet Gynecol Sci. 2016;59(5):415-20.
[22] Erb-Eigner K, Willerding G, Taupitz M, Hamm B, Asbach P. Diffusion-weighted imaging of ocular melanoma. Invest Radiol. 2013;48(10):702-07.
[23] Liu QY, Zeng YP, Lin XF, Liu ZF, Wu XF, Li HG. MRI findings in primary vaginal melanoma-a report of fthis cases. Clin Imaging. 2015;39(3):533-37.

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