Characteristic findings of malignant melanoma in the sinonasal cavity on magnetic resonance imaging

XU Qing-gang, FU Li-ping, WANG Zhen-chang, XIAN Jun-fang, HE Li-yan, ZHANG Zheng-yu and LIU Cheng-yao

Keywords: malignant melanoma; nasal cavity; magnetic resonance imaging

Background Malignant sinonasal melanoma (MSM) is a rare tumor with a perplexing signal intensity due to variable histopathologic components. This study was undertaken to delineate its MR imaging features.

Methods MR imaging findings of 10 patients (6 women and 4 men, mean age 61.3 years old) with pathologically confirmed MSM were retrospectively reviewed. The location, size, signal intensity, enhancement, and internal imaging characteristics of all tumors were evaluated. Signal intensity and degree of enhancement was graded in comparison with the gray matter and adjacent muscle uptake, respectively.

Results There were 8 tumors that were pathologically confirmed to contain melanin. Compared to gray matter of the brain, 7 of them demonstrated hyperintensity on T1WI and 6 (6/7) showed hypointensity on T2WI. There was multiple linear, dark-signal intensity on T2WI within the mass in 9 of the 10 patients’ tumors. Evaluated with gadolinium-enhanced imaging, all 10 patients showed moderate enhancement within the areas that were isointense in the lesion on pregadolinium T1WI. Moreover, some parts which displayed hyperintensity on T1WI within the tumors of 7 patients showed mild enhancement that was similar to muscle on a time-intensity curve (TIC).

Conclusions MSM shows characteristic MR signal intensity (hyperintensity on T1WI and the linear, low-signal intensity on T2WI), which may provide valuable information for clinical diagnosis. Together with conventional MRI, TIC may be useful for indicating pleomorphic patterns of MSM.

Primary mucosal malignant melanoma in the nasal cavity and paranasal sinuses is a rare entity with equal frequency in elderly adults of both sexes,1,2 and it is the relative inaccessibility of the mucosa to self-examination compared to easily found tumors on the skin that often delays diagnosis. Sinonasal melanomas originate from melanocytes that have migrated during embryological development from the neural crest to the mucosa of the nose and sinuses. The most frequent site of origin is the nasal septum,3 closely followed by the lateral nasal wall and the middle and inferior turbinates.4 However, in many ways typical malignant melanomas arise from the paranasal sinuses. The most common sinus involved is the maxillary antrum.5 Unfortunately, there is a frequent problem that the lesions in some cases are too extensive to determine the exact site of origin. The symptoms of nasal melanoma are often nonspecific, and it may be unilateral nasal obstruction and epistaxis,6 resulting in pain and facial deformity in advanced cases. So early detection is crucial for longer patient survival, diagnosis and treatment.

The mainstay of treatment for nasal melanomas is surgical resection with clear margins.4,6 However they are usually clinically indistinguishable from the more common nasal polyposis and sinusitis that can be relieved by the means of partial resection. Because there are dramatically different categories of surgeries for melanoma and benign growths, such as nasal polyposis and sinusitis, it is urgent for researchers employing preoperative MR imaging to define a limited subset of patients with a high likelihood of nasal melanoma.

It is known that nasal melanoma contains the paramagnetic property of melanin pigment that appears with characteristic hyperintensity on T1WI and hypointensity on T2WI, which may help establish this diagnosis in many cases on the basis of preoperative MR imaging.7,8 However hemorrhage and other substances in some cases masquerade as melanin and may be indistinguishable in differential diagnosis. In addition, some cases of melanoma (such as amelanotic melanoma), with no characteristic melanin signal on MR imaging, are similar to more common tumors in the sinonasal cavity and difficult to differentiate from them. All these difficulties motivated us to design a retrospective series to
better delineate the MR imaging features of nasal melanoma worthy of investigation in a future differential diagnostic study.

**METHODS**

An electronic medical record review, approved by the Institutional Review Board in Beijing TongRen Hospital, Capital Medical University, revealed 10 patients who presented with pathologically confirmed malignant melanomas of the sinonasal cavity between 2004 and 2011. The series included 4 men and 6 women whose ages at the time of diagnosis ranged from 39 to 73 years old with a mean age of 61.3 years old (Table 1). They presented mostly with unilateral nasal obstruction and epistaxis, two of which accompanied with facial numbness.

Available MR imaging data were acquired for all 10 patients. All patients had undergone sinus MR imaging with 8-channel head coil, performed on a 1.5T MR imaging scanner (Signa TwinSpeed; GE Healthcare, Milwaukee, Wisconsin). Participants lay supine inside the scanner and their heads were restrained with padding behind the neck. During the whole scan process, subjects were required to stay still. The standard institutional sinus imaging protocol used in all patients included high-resolution spin-echo (SE) T1WI and fast spin-echo (FSE) T2WI with 0.5 mm spacing, 5 mm sections, 2–4 number of excitation (NEX), 180 × 220 mm field of view (FOV), and a 256 × 256 matrix. SE T1WI parameters were the following: time of repetition (TR) 400.0–600.0 ms, time of echo (TE) 15.0–20.0 ms. FSE T2WI acquisition parameters were TR 2000.0–4000.0 ms, and TE 80.0–120.0 ms. Pregadolinium T1WIs and T2WIs in two planes (axial plus coronal or sagittal) and frequency-selective fat-suppressed axial postgadolinium T1WIs were acquired in all patients. Gadopentetate dimeglumine (0.1 mmol/kg, Magnevist; Bayer Schering Pharma, Berlin, Germany) was injected at a rate of 2.0 ml/s through a 21-gauge intravenous line with a power injector. Before postcontrast MR images were obtained, 7 patients underwent dynamic contrast enhancement (DCE)-MR imaging employing 3D-fast spoiled gradient echo (FSPGR), for which the acquisition parameters were the following: TR 8.4 ms, TE 4.0 ms, flip angle 15°, FOV 220 × 220 mm, matrix size 256 × 160, slice thickness 3.2 mm with 0 spacing and 5 minutes acquisition time. During DCE-MRI, twelve sequential 13-second images with 12-second intervals were acquired as follows: one control image before injection of contrast agent and 11 images during and after injection. The time-intensity curves (TICs) were used for analyzing whether the lesions with high-signal intensity on pre-contrast T1WI were enhanced or not. However the enhancement patterns were not included in the evaluation considered.

MR findings of the tumor were predominately evaluated for the following features—the location, size, signal intensity, enhancement, and internal imaging characteristics. The signal intensity of the tumor relative to that of the gray matter was graded as hyperintense, hypointense, and isointense on the T1- and T2-weighted images. DCE-MR imaging of the tumor was evaluated by using an AW 4.2 workstation (GE Healthcare). Data analysis of contrast enhancement on dynamic images was performed with a region of interest (ROI) technique. A ROI was drawn manually for signal intensity measurement and was approximately 10 mm² in area in each patient. The signal enhancement of the lesion was evaluated by comparison with adjacent mucosa and muscle uptake. Tumor uptake as remarkable as that of adjacent inflamed mucosa was evaluated as marked enhancement. Tumor uptake similar to that of muscle was evaluated as mild enhancement. Tumor uptake between that of muscle and inflamed mucosa was evaluated as moderate enhancement.

The MR images were evaluated by two experienced radiologists who had more than 10 years of practice and training in head and neck imaging. Histopathologic findings were reviewed with special attention given to melanin in the tumors. Hemorrhage was not evaluated in this study because surgery-related blood was not clearly

<table>
<thead>
<tr>
<th>Cases</th>
<th>Age/sex</th>
<th>Primary location</th>
<th>Tumor size (cm)</th>
<th>Characteristic signal findings</th>
<th>Histopathologic findings melanin</th>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>T1WI</td>
<td>T2WI</td>
</tr>
<tr>
<td>1</td>
<td>73/F</td>
<td>Left nasal cavity</td>
<td>5.6×4.9×2.0</td>
<td>Hetero</td>
<td>Hetero</td>
</tr>
<tr>
<td>2</td>
<td>67/F</td>
<td>Right maxillary sinus</td>
<td>3.9×3.8×2.7</td>
<td>→</td>
<td>→</td>
</tr>
<tr>
<td>3</td>
<td>60/F</td>
<td>Left maxillary sinus</td>
<td>5.4×4.6×4.5</td>
<td>Hetero</td>
<td>Hetero</td>
</tr>
<tr>
<td>4</td>
<td>68/M</td>
<td>Right ethmoid sinus</td>
<td>3.0×2.4×1.5</td>
<td>Hetero</td>
<td>Hetero</td>
</tr>
<tr>
<td>5</td>
<td>63/F</td>
<td>Right maxillary sinus</td>
<td>4.6×4.4×4.1</td>
<td>Hetero</td>
<td>Hetero</td>
</tr>
<tr>
<td>6</td>
<td>71/M</td>
<td>Left nasal cavity</td>
<td>0.6 (diameter)</td>
<td>↑</td>
<td>→</td>
</tr>
<tr>
<td>7</td>
<td>63/F</td>
<td>Left nasal cavity</td>
<td>5.2×3.8×3.1</td>
<td>Hetero</td>
<td>Hetero</td>
</tr>
<tr>
<td>8</td>
<td>59/M</td>
<td>Left nasal cavity</td>
<td>2.1×2.0×1.8</td>
<td>→</td>
<td>→</td>
</tr>
<tr>
<td>9</td>
<td>50/M</td>
<td>Bilateral frontal sinus</td>
<td>5.1×3.5×1.9 Hetero</td>
<td>Hetero</td>
<td>Mo</td>
</tr>
<tr>
<td>10</td>
<td>39/F</td>
<td>Left nasal cavity</td>
<td>4.4×1.6×2.3</td>
<td>Hetero</td>
<td>Hetero</td>
</tr>
</tbody>
</table>

↑, hyperintense; →, isointense; ↓, hypointense; +, moderate; + + +, abundant; →, none. E, enhancement; Hetero, heterogenous; NA, not available; Mi, mild; Mo, moderate; Y, yes; N, no.

Table 1. Summary of MR and histopathologic findings (melanin) of the patients with malignant melanoma of the sinonasal cavity
differentiated from hemorrhage in the tumors.

RESULTS

Table 1 provides the MR and histopathologic details of the patients with malignant melanoma of the sinonasal cavity. The tumors appeared to be primarily located in the nasal cavity \( (n=5) \) and the maxillary sinus \( (n=3) \), with one in the ethmoid sinus, and one in the frontal sinus. In patients 1, 2, 3, 5, 7 and 10, the involved sites were the ipsilateral nasal cavity, maxillary sinus, orbit, and soft tissue beyond the bony wall of the maxillary sinus. Moreover, the ipsilateral pterygopalatine fossa was also involved in patient 7. In patients 4 and 9, the right orbit, right (or bilateral) ethmoid sinus and right (or bilateral) frontal sinus were involved. In patient 8, the region of choana narium was the site of the tumor, and the posterior of the nasal septum was involved. The tumors were mostly lobulated and displayed an aggressive, expansive growth pattern. However, in patient 6, the tumor was too small to involve any peripheral structure, and was confined to the left middle nasal meatus. The size of each mass was variable, ranging from 0.6 to 5.6 cm.

On T1 WI, 7 tumors (6 melanotic tumors and one amelanotic tumor) were heterogeneous and one melanotic tumor was homogeneous, all of which were hyperintense relative to the gray matter of the brain (Figure 1A and 1C). Two tumors, one melanotic tumor and one amelanotic tumor, appeared to be isointense. On T2WI, one case of amelanotic melanoma displayed hypointensity, and 6 melanotic melanoma displayed hypointensity (Figures 1B and 2A). Tumors were homogeneously isointense in two cases with melanotic melanoma and one with amelanotic melanoma. There was multiple linear, dark-signal intensity on T2WI within the mass (Figures 1B and 2A) in all patients except for patient 6.

Evaluated with gadolinium-enhanced imaging, all 10 patients showed moderate enhancement within the areas that were isointense in the lesion on pregadolinium T1WI, and multiple enhanced linear structures within the mass in 9 patients (Figures 1D, 2B and 2C). Moreover, some parts which displayed hyperintensity on T1WI within the tumor in 6 patients showed mild enhancement as similar to muscle (Figure 1E and 1F).

DISCUSSION

MSM is an extremely rare tumor which may display a racial discrepancy and is reported in the literature to be more common in Caucasians. Because of the limited number of studies and the lower incidence in Asians, especially in Chinese, it is difficult to ascertain whether the risk differs from that found in Caucasians. The mean age of onset we found, 61.3 years old, is consistent with the previous report. And it was reported that younger

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Figure 1. Melanotic melanoma in a 63-year-old woman (patient 7). A: The axial T1-weighted image shows a large mass, being heterogeneous, consisted of hyperintense components to gray matter of the brain in the left maxillary sinus and nasal cavity. It appears that the lesion in the front of left nasal cavity (arrow) has higher signal intensity than the part in the left maxillary (arrow). B: On T2WI, the corresponding parts are isointense (arrow) and hypointense (curved arrow) and multiple linear-dark signals (curved arrow) are also seen within the mass. C: Coronal T1WI (C) delineates the contour of tumor better. D: Gadolinium-enhanced coronal image shows heterogeneous enhancement of the mass with multiple enhanced linear structures (arrows) within the mass. The high signals on T1WI are indistinguishable from each other. E: MRI dynamic enhancement overlay. ROI 1 (melanin) which shows mild enhancement over time is similar to ROI 3 (muscle), and ROI 2 shows no enhancement at all. F: DIC of DCE-MRI. G: Histopathologic examination of the mass shows tumor section containing melanin pigment (arrow) and intratumoral vessels (curved arrow) (Hematoxylin & eosin staining, original magnification×10).
patients generally had a better prognosis because of better immunosurveillance. Although sinonasal malignant melanoma more frequently arises in the nasal cavity than in the paranasal sinuses, in certain circumstances the maxillary antrum is the most likely origin. The site of the primary tumor might also be a prognostic factor, and patients with the paranasal sinus melanoma have a higher mortality than those who have the nasal cavity as the primary site.

Nasal bleeding with unilateral nasal obstruction is the most common presenting symptom. Others include deformity of the nose, cheek swelling, hyposmia, facial pain, and visual disturbance in the advanced cases. These clinical presentations are nonspecific, and easily confused with nasal polyposis and sinusitis, especially for patient 6 in this study. The diagnosis of melanoma in the nasal cavity may be quite difficult and delayed, especially in patients in whom the lesion is not pigmented. This emphasizes both the present need to better define the appearance of, and increase physician awareness of, melanoma within the differential diagnosis of sinonasal masses. It also suggests a clear need for continuing investigation of complementary noninvasive imaging techniques, including MR imaging methods that can differentiate melanoma from the more common nasal diseases.

The typical signal intensity characteristics of melanoma elsewhere in the body have been documented. The appearance of melanotic melanoma is high signal intensity on T1WI and low signal intensity on T2WI. It depends on how much melanin is present; the greater the concentration of melanin in the tumor, the higher the signal intensity on T1WI and the lower the signal intensity on T2WI. In our study, 7 tumors which were confirmed to contain melanin by histology demonstrated hyperintensity relative to the gray matter of the brain on T1WI. It appears that the T1 shortening effect is mainly due to melanin, and the amount of melanin pigment in the lesion varies considerably from tumor to tumor, and also within the same tumor. Moreover the products of hemorrhage may partially contribute to this effect. Besides, this effect may also be correlated with the wide range of repetition times and echo times used in the acquisition sequences.

There was linear low-signal intensity on T2WI and multiple enhanced linear structures within the mass in all cases except for patient 6 in this study. The literature has documented that these signs correspond with intratumoral vessels, representing a rich vascular network within the mass. It also suggests that a fibrous septum consisting of fibroblast, capillaries and abundant collagen is found in the tumor. This additional feature within a lesion can make melanoma the most likely diagnosis, especially when a lesion lacks pigmentation; which may include one-third of sinonasal melanomas.

Evaluated with contrast-enhanced MRI, TIC showed moderate enhancement within the areas that were isointense on pregadolinium T1WI; this may be correlated with the microscopic spindle-cell patterns in melanoma. This finding may help to differentiate MSM from hypovascular tumors arising in the sinonasal cavity. However, the pattern of enhancement of MSM was uncertain because of the rare sinonasal origin and the limited number of cases.

There are several substances that show hyperintensity on T1WI on pregadolinium imaging besides melanin; such as hemorrhage, hyperproteinaceous secretions, fungus, paramagnetic materials, and fat. Fat tissues can be easily identified by use of fat-suppressed imaging. There may be hemosiderin deposits around a progressing hemorrhage. Lesions containing hyperproteinaceous secretions, fungus and hemorrhage would usually not enhance in a solid fashion, and inflamed mucosa in a peripheral pattern would be displayed. But how can we determine if they have enhancement or not on post-gadolinium imaging? TIC of DCE-MRI may be particularly useful to solve this problem, as these substances would not be enhanced at all on TIC. On the contrary, parts of the tumor (representing melanin) which displayed hyperintensity on T1WI within the tumor in 7 patients in this study showed mild enhancement that was similar to muscle on TIC, which is consistence with previously reported melanoma in the retinal choroids. It has suggested that the degree of endovascular permeability of the intrinsic tumor vascularity could be estimated by this method.
Therefore, this finding can be used to predict pleomorphic patterns of the tumor and help evaluate the nature of the tumor.

The major weakness in this study was that we could not directly correlate the MR findings with the surgical features because the specimens were fragmented during the endoscopic procedure. Another potential weakness of the study was that the number of cases was too small to provide definitive quantitative estimates of MSM. Our conclusions need to be further evaluated after collecting data from more patients with MSM.

Sinonasal melanoma is an uncommon malignant entity with perplexing signal intensity due to variable histopathologic components, and it should be included in the differential diagnosis of masses in the sinonasal cavity when a lobular mass with a high signal intensity on T1WI and low signal intensity on T2WI is detected on MR imaging. Because these characteristics may not be easily distinguishable on MR images, and less pigmented-melanin lesions may be mistaken for the more distinguishable on MR images, and less pigmented-melanin lesions may be mistaken for the more common nasal polyposis and sinusitis which are treated differently, this retrospective study indicates that the multiple linear, low-signal intensity on T2WI and mild enhancement lesions that displayed hyperintense on precontrast T1WI on TIC should be born in mind for a melanoma diagnosis.

REFERENCES