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Title page

Title: Neurocutaneous melanosis and negative fluorodeoxyglucose positron emission tomography.

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Abstract:

Neurocutanous melanosis is a rare condition characterized by cutaneous melanocytic nevi and the presence of melanocyte in the leptomeninges. It is commonly associated with malignant melanoma formation in central nervous system (CNS) with poor prognosis. Here we report a 13-year old boy with neurocutaneous melanosis presented with seizure with diffuse CNS malignant melanoma as demonstrated by MRI. 18F-fluorodeoxyglucose positron emission tomography (PET) was performed but was unable to pick up the CNS involvement. So far, this is the first report involved the use of PET in neurocutaneous melanosis and we suggest MRI is more sensitive than PET with 18F-fluorodeoxyglucose in such condition.

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Introduction

Neurocutaneous melanosis (NCM) is a rare condition characterized by cutaneous giant melanocytic nevi and melanocyte in the leptomeninges. Diagnosis of NCM is made through both clinical findings of giant congenital naevus and radiological evidence of leptomeningeal melanosis. With the increasing use of positron emission tomography (PET), here we report the presentation of this condition together with the PET findings.

History

Our patient was a 13 year-old boy with good past health and family history of breast cancer. He presented in June of 2006 with 1-month history of headache followed by acute confusion and an episode of generalized tonic clonic seizure. Physical examination found a 10-cm sized hairy melanocytic naevus over right temporal-parietal region and right homonymous hemianopia. Plain computer tomography (CT) brain showed communicating hydrocephalus and a 1.4cm hyperdense lesion over the left medial temporal lobe without surrounding edema. Magnetic resonance imaging (MRI) showed the lesion was T1-hyperintense T2-isoinense with gadolinium contrast enhancement. There was no leptomeningeal enhancement. MRA and CTA were unremarkable. Blood tests and CSF exam were normal. Ventriculo-peritoneal shunting was performed for hydrocephalus. The family opted for conservative treatment for the lesion.

MRI brain one month later showed increase in size of lesion with diffuse leptomeningeal enhancement. MRS showed increased choline peak and decreased N-acetylaspartic acid peak suggested a neoplastic process.

Craniotomy and gross total resection of the tumour mass with biopsy of naevus were performed. The dura was dark-grey in colour. Histopathology revealed the tumour composed of epithelioid cells containing melanin with high nuclear/cytoplasm ratio, enlarged nuclei and prominent nucleoli. Diagnosis of malignant melanoma was made and confirmed by positive HMB45 and S-100 immunohistochemical staining. Proliferative marker (MIB1) confirmed high proliferation rate. Naevus biopsy showed congenital naevus with no evidence of malignancy.

MRI of the spinal cord performed on post-operative day 17 showed diffuse enhancement with nodular thickening throughout the whole thecal sac that was compatible with diffuse CSF seedling. There was also encasement of cervical and proximal thoracic cord. Contrary, whole body PET with 18F-fluorodeoxyglucose(FDG) on the day after MRI exam could not show metastasis apart from post-operative changes (Fig. 1).

Palliative chemotherapy with tamozolamide and radiotherapy were planned. Repeat CT brain showed new tumour deposit posterior to operative site with severe cerebral edema. His condition remained critical due to repeated seizure and finally passed away in August, 2006.

Discussion

Kadonaga and Frueden [1] defined NCM that includes

1. Large (>20 cm largest adult diameter) or multiple (3 or more) congenital nevi in association with meningeal melanosis or melanoma. Infant lesion diameters of 9 cm on the head and 6 cm on the body are accepted because the projected growth of the lesion surface area is assumed to be proportional to normal skin growth of the body region it lies within.

2. No evidence of cutaneous melanoma except when examined areas of meningeal lesions are histologically benign.

3. No evidence of meningeal melanoma except when examined cutaneous lesions are histologically benign.

The disease is not hereditary and affects both sexes equally without definite risk factor. Most patients presented at young age with hydrocephalus and seizure. Contrary, there are a few reported cases presented in adulthood up to age 65. Around 8-10% of NCM are associated with Dandy-Walker complex.

Radiological diagnosis

Diagnosis of NCM required both clinical and radiological findings that MRI plays an important role. Melanosis presents with T1 shortening with homogeneous gadolinium enhancement, and intermediate signal on T2-weighted images. However, variations had been reported with slightly hyperintense in T2-weighted images and hypointense on T1-weighted images for amelanotic melanoma.

PET with FDG is effective in detection of extracranial malignant melanoma and superior to CT alone, while combining the two modalities, PET/CT was shown to be even more superior [2, 3]. Contrary, it had limitations in detecting brain metastasis, small lung nodules and lesions less than 10mm [4]. As a result, it is more useful for American Joint Committee on Cancer (AJCC) melanoma stage III and IV disease. One study comparing PET/CT with FDG and whole body MRI for advanced melanoma showed PET/CT had higher accuracy of 86.7% compared to that of MRI 78.8%, especially in terms of N-staging and detection of skin metastases, while MRI was more sensitive for liver, bone and brain metastasis [5]. Another study used both PET/CT and MRI for monitoring of progress of melanoma having

chemotherapy treatment. Out of their 11 patients who had brain metastases, 9 of them were first picked up by MRI or contrast CT, only the rest of the two picked up by PET/CT. And the author emphasized that MRI should be used for detecting cerebral melanoma metastases for high risk patients [6]. Despite the relatively lower sensitivity for brain metastases, PET/CT was sensitive enough for extracranial disease monitoring that correlated well with clinical outcome after chemotherapy [6]. So far, there is no reported use of PET for NCM or melanosis. In our patient PET failed to demonstrate the diffuse CNS involvement that was shown by MRI. Despite NCM gives rise to melanoma, since the numbers of reported cases were limited, it is difficult to say if the behaviour of melanomas arising from NCM is same or different to those originated extracranially with cerebral metastases. Tumour characteristic is important in the current discussion as PET using FDG depends on the metabolic activities. Difference in terms of tumour nature, if exist, may affect the uptake of FDG and so the sensitivity of PET. Based on the result from cerebral metastases of melanoma and our current reported experience, MRI should be the first line imaging modality from diagnosis to subsequent treatment monitoring for NCM. But PET/CT may still play a role in excluding extracranial melanoma deposits as it is more sensitive to whole body MRI as extrancranial melanoma deposits almost exclude the diagnosis of NCM according to the definition.

Despite there were a number of studies showing that PET with FDG was not very sensitive for cerebral metastasis of melanoma, there was no definite research or study addressing the reason behind. One of the purposed reason is that brain has high consumption of glucose and result in a strong background signal. High metabolic rate tissues like metastatic tumour, especially the small one, would be difficult to trace from this background [7]. The answer for this may be using isotopes more specific for tumour.

Impact to current clinical practice

Our patient developed diffuse leptomeningeal enhancement in MRI within 2 months and died within 3 months from presentation. It was suggested presence of giant congenital naevus should raise the suspicious of NCM and regular monitoring may be indicated. But the risk of having NCM and subsequent CNS melanoma was low upon 5 years follow up [8]. Moreover, this might not be feasible as leptomeningeal enhancement might occur at late stage with rapid progression. This implies early diagnosis of NCM is difficult. We suggest for patient with giant naevus, especially children as NCM mostly found in young patients, at least they should have regular clinical monitoring of the size of the naevus and new neurological symptoms. New abnormal behaviour or neurological deficits should raise the suspicious and urgent MRI brain is needed. They may also indicated for serial MRI brain but may be of low yield as mentioned previously, as well as for early biopsy for any subtle radiological change or development of definite nodule.

The false negative of PET in our patient suggested monitoring of CNS disease progression should base on clinical features and MRI. But PET may be useful for detecting extracranial involvement as peritoneal seeding could occur if ventriculoperitoneal shunt was inserted [9]. Also it is worth to note that our observation on PET was based on FDG, employing other isotopes may be different.

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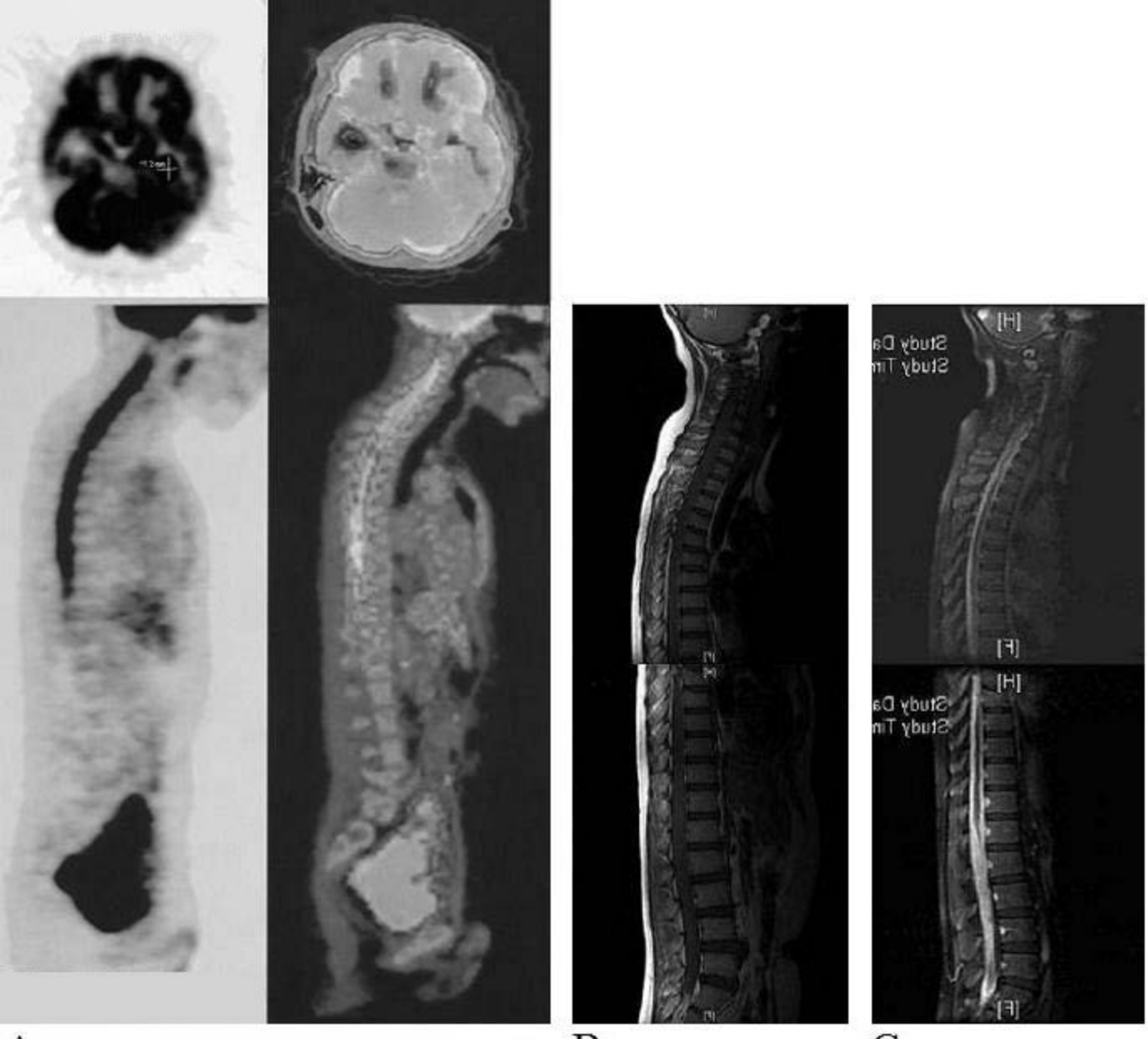

A B C

Legends

Figure 1. A, PET scan of brain and spinal cord without evidence of metastasis. B, T1-weighted image of whole spine. C, T1-weighted image with diffuse contrast enhancement and nodular thickening throughout whole thecal sac.