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Neurocutaneous Melanosis with an Intracranial Cystic-Solid Meningeal Melanoma in an Adult: A Case Report and Literature Review of 21 Similar Cases

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Abstract

BACKGROUND

Neurocutaneous melanosis (NCM) is a rare congenital, nonhereditary neurocutaneous syndrome that mainly occurs in children; adult NCM is very rare. Due to its rarity, the clinical features and treatment strategies for NCM remain unclear. The purpose of this study was to explore the clinical features, diagnosis, treatment and prognosis of NCM in adults. Most intracranial meningeal melanomas are solid masses, and cystic-solid malignant melanomas are very rare. Due to the lack of data, the cause of cystic changes and the effect on prognosis are unknown.

CASE SUMMARY

A 41-year-old woman was admitted to the hospital with intermittent headache for 1 mo. Magnetic resonance imaging (MRI) showed a 4.7×3.6 cm cystic-solid mass in the left temporal lobe with peritumoral edema. The entire mass was removed, and postoperative pathology indicated malignant melanoma.

CONCLUSION

MRI is the first-choice imaging approach for diagnosing central nervous system diseases in NCM patients, although cerebrospinal fluid may also be used. At present,

there is no optimal treatment plan; gross total resection combined with BRAF inhibitors and MEK inhibitors might be the most beneficial treatment.

Key Words: Neurocutaneous melanosis; Meningeal melanoma; Central nervous system disease; Adult; Cystic-solid tumor

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Core Tip: Neurocutaneous melanosis (NCM) is a rare congenital, nonhereditary neurocutaneous syndrome that mainly occurs in children, while adult NCM is very rare. Due to its rarity, clinical features and treatment strategies for NCM remain unclear. Herein, we report a case and review such reports and explore the clinical features, diagnosis, treatment and prognosis of NCM in adults.

INTRODUCTION

Neurocutaneous melanosis (NCM) is a rare congenital, nonhereditary neurocutaneous syndrome. Specifically, NCM is a rare combined abnormality of the skin and central nervous system (CNS)^[1], mainly presenting as congenital melanocytic nevi with benign or malignant melanoma of the central nervous system^[2]. NCM is a neuroectodermal dysplasia⁸ believed to arise from an embryological defect in the migration of melanoblasts from the neural crest to the leptomeninges and skin^[3]; it was first described by Rokitanski in 1861^[4]. Patients with NCM usually have neurological symptoms at an early age. Most patients have a poor prognosis once symptoms occur, regardless of whether the CNS tumors are benign or malignant; in most cases, the disease is fatal within 3 years of onset^[5]. Primary malignant melanoma in the central nervous system is usually a single solid mass, and melanoma with large cystic changes is extremely rare. Here, we describe a rare adult NCM complicated with intracranial

cystic-solid malignant melanoma and review the relevant literature to discuss the clinical features, diagnosis, treatment and prognosis.

CASE PRESENTATION

Chief complaints

The patient was admitted to our department with intermittent headache for 1 ¹¹mo

History of present illness

A 41-year-old woman was admitted to the hospital with intermittent headache for 1 mo. The headache could not be relieved by rest. There were no obvious symptoms of nausea, vomiting and epilepsy.

History of past illness

The patient was born with diffuse melanosis of the skin, mainly covering the back of the trunk, shoulders and neck, with multiple satellite nevi on the limbs and a few hairs on the surface of the nevi in the first few years after birth (figure 1F). The lesion was considered to be a birthmark and had not been treated. No malignant clinical signs, such as enlargement, ulcers, bleeding or itching, were observed in the pigmented area as the patient aged.

Personal and family history

¹ There was no past history of skin or CNS disease or malignant tumor, The patient had no history of surgery, and her parents and children had no history of congenital nevi or melanoma.

Physical examination

The patient has diffuse melanosis of the skin, mainly covering the back of the trunk, shoulders and neck, with multiple satellite nevi on the limbs and a few hairs on the

surface of the nevi. Examination of her nervous system revealed no obvious abnormalities.

Laboratory examinations

Laboratory examinations such as routine blood tests, routine urine tests and blood biochemistry were normal. The pathological results showed malignant melanoma. Immunohistochemistry results were as follows: Ki-67 (+30%), S-100 (+), HMB45 (+), Vimentin (+); all other markers were negative (figure 2).

Imaging examinations

MRI examination of the head revealed a mass with intramural cysts located on the left temporal lobe. The solid part of the tumor was hyperintense on T1-weighted images and hypointense on T2-weighted images, and the cystic components showed the opposite. The lesion had a clear boundary of approximately 4.7*3.6 cm and was surrounded by peritumoral edema (figure 1A, B). After the injection of a contrast agent (Gd-DTPA), obvious heterogeneous enhancement was observed in the solid part, while the cystic part showed abnormal ring-shaped enhancement (figure 1C, D, E).

FINAL DIAGNOSIS

We ultimately diagnosed this patient with NCM with meningeal melanoma.

TREATMENT

The patient underwent surgery to remove the intracranial mass after admission. During the operation, the tumor appeared blackish brown (the peripheral leptomeninges were also stained black), with light-yellow sac fluid inside, and the blood supply to the tumor was extremely rich. First, the cystic fluid was drawn out, and the lesion was then gradually separated along its periphery until it was completely removed. The pathological results showed malignant melanoma. Immunohistochemistry results were

as follows: Ki-67 (+30%), S-100 (+), HMB45 (+), Vimentin (+); all other markers were negative (figure 2).

OUTCOME AND FOLLOW-UP

The patient was in good condition after the operation; she refused further radiotherapy and chemotherapy and was discharged on the tenth day after the operation. Five months after the operation, the patient went to a local hospital due to unconsciousness after severe headache and died of ineffective treatment. Her death was considered to be due to obstructive hydrocephalus from tumor progression.

DISCUSSION

We report an adult female patient with a congenital melanocytic nevus (CMN) on her neck, shoulder and back. A space-occupying lesion in the left temporal lobe was found during a magnetic resonance imaging (MRI) scan of her head. The tumor was resected en bloc under microscopy, and subsequent histopathology and immunohistochemistry analyses revealed malignant melanoma. In PubMed, we searched for adult NCM cases published between 1990 and 2020. "Neurocutaneous melanosis" was used as the key word and "Adult: 19 + years" as the qualification, and reports without detailed clinical data were excluded. In addition, references cited in selected articles were manually searched and reviewed to identify other potentially eligible studies. Patient data were extracted, and the clinical data were described and analyzed.

According to previous reports, patients with NCM generally develop neurological symptoms at an early age, and most of them die within 3 years after the onset of symptoms. Adult NCM is very rare [5]. The vast majority of patients with NCM are sporadic cases, with few familial cases being reported. Approximately 2/3 of patients with NCM have a giant CMN, and the remaining 1/3 have multiple small lesions [12]. Patients with a giant CMN located on the posterior axis of the trunk and multiple satellite nevi are at higher risk for NCM [13]. The current diagnostic criteria for NCM were revised by Kadonaga *et al* in 1991 [14] as follows: 1. Large or multiple congenital

nevi are observed in association with meningeal melanosis or melanoma. Large refers to a lesion size equal to or greater than 20 cm in diameter in an adult; in neonates and infants, large is defined as a size of 9 cm in the head or 6 cm in the body. Multiple signifies three or more lesions. 2. There is no evidence of cutaneous melanoma, except in patients in whom the examined areas of the meningeal lesions were histologically benign. 3. There is no evidence of meningeal melanoma, except in patients in whom the cutaneous lesions were histologically benign. According to the above criteria, our patient was diagnosed with NCM. As NCM is very rare, there is no specific incidence. Men seem to be more susceptible to the disease than women, or it is possible that male patients have a greater chance of surviving to adulthood than female patients.

Most intracranial meningeal melanomas are solid masses, and some tumors may have small necrotic cysts inside; cystic-solid malignant melanoma is very rare. In the literature, there were 2 patients with similar lesions. Kang, S.G. *et al* ^[15] reported a patient with NCM who had a cystic-solid meningeal melanocytoma in the left temporal lobe, a dermoid cyst in the right temporal lobe, and Dandy-Walker syndrome. Ma, Mian *et al* ^[16] reported a patient with NCM who had cystic-solid malignant melanoma in the left temporal lobe and survived for 22 mo after partial resection of the tumor. Combined with our patient, melanoma with large cystic degeneration occurred only in adult patients, and whether tumors were benign or malignant did not seem to have an absolute relationship with cystic degeneration. Due to limited data, it is impossible to clarify the impact of cystic changes in NCM intracranial tumors on the prognosis of patients.

In general, when a cystic mass develops in the central nervous system, the cystic component is caused by tumor necrosis or degeneration. The tumor cyst of our patient was mainly filled with a light-yellow liquid. In the literature, we found that the cysts of some tumors may constitute a nutrient reservoir for brain tumors to ensure that tumor metabolism and tumor cell synthesis can be carried out. Through a component analysis, serum was reported as one of the possible sources of nutrients in most cystic fluids, which may be due to the destruction of the blood-brain barrier by the tumor ^[17].

Clinical presentations of NCM are nonspecific and vary depending on the tumor site, size and invasion site; these mainly include epilepsy, intracranial hypertension, dyskinesia, and hydrocephalus.^[9] Hydrocephalus has been reported in approximately two-thirds of cases and occurs as a result of the obstruction of cerebrospinal fluid (CSF) flow due to melanotic infiltration of arachnoid villi and leptomeninges^[12]. Based on our data, the incidence of hydrocephalus in adults was 42.8%. According to this set of data, the peak of neurological symptoms in adult patients is in the third 10 years of life. In addition, the association between Dandy-Walker syndrome and NCM is rare and complex. It has been reported that approximately 8%-10% of cases of Dandy-Walker syndrome are related to NCM^[18]. There are currently two theories describing the connection between NCM and Dandy-Walker syndrome. It is thought that melanotic infiltration interferes with the capacity of primitive meningeal cells to induce the normal migration of neurons, deposition of extracellular matrix, and development of normal CSF pathways, leading to posterior fossa cyst formation and vermian dysgenesis. Alternatively, Barkovich *et al* suggested that melanosis interferes with the ectodermal-mesodermal interaction, causing an abnormal formation of the fourth ventricle and cerebellum^[19].

Some literature reports have shown that when intracranial lesions of NCM manifest as solid melanoma foci, they are usually asymptomatic^[20]. When solid lesions involve the amygdala, pons, and cerebellum, most have a stable or benign course until they develop into malignant melanoma^[21]. This may be one reason why NCM does not develop in some patients until adulthood.

At present, MRI is the first-choice imaging approach for diagnosing central nervous system diseases in NCM patients, although it cannot distinguish benign and malignant intracranial tumors.^[6] In fact, as melanin pigment is inherently paramagnetic, typical NCM lesions usually exhibit high intensity on T1-weighted images and low intensity to isointensity on T2-weighted images^[22]. Due to differences in the melanin content,^[3] intracranial melanomas are divided into the melanin type, nonmelanin type, mixed type (melanin type plus nonmelanin type) and blood type according to MRI characteristics

[23]. Because NCM does not have a unique clinical manifestation, patients with a giant CMN without neurological symptoms should be examined regularly to rule out the disease. It has been reported that the most common melanin deposits occur in the temporal lobe (especially the amygdala), cerebellum and pons [24]. However, lesions were found in the frontal lobe of some patients, as revealed by our analysis.

There are reports in the literature indicating that CSF can also be used to diagnose NCM. Kolin, D. L. *et al* reported on a patient they diagnosed with CSF, which they claimed was ⁵ the first case report of a diagnosis of primary leptomeningeal melanomatosis (PLM) with an NRAS mutation using a CSF sample for both confirmatory immunocytochemistry and molecular testing [25]. However, in regard to the diagnosis of NCM, we believe that imaging examinations have the advantages of convenience and noninvasiveness. As a result, diagnostic imaging is still the first choice, and CSF examination can be used to further determine whether the lesion is benign or malignant.

¹ Due to the rarity of NCM, a standard treatment approach for this disease has not yet been established. The current treatment options are mainly microsurgery, chemotherapy, immunotherapy, gene therapy, ventricular-peritoneal shunt and comprehensive treatment. However, melanoma in some patients is diffuse and cannot be removed surgically, and it seems that the effects of radiotherapy and chemotherapy cannot effectively extend the life of patients. In the current study, mutations in codon 61 of the NRAS gene were found in most cases. ⁵ However, there are currently no established targeted therapies for patients with NRAS-mutated melanomas; BRAF inhibitors and MEK inhibitors may be used for treatment, but their effects and safety remain to be determined [26].

³ Neurocutaneous melanosis usually has a very poor prognosis. The 2016 classification by the World Health Organization categorizes central nervous system melanocyte lesions into meningeal melanocytosis, meningeal melanomatosis, meningeal melanocytoma and meningeal melanoma, where meningeal melanocytosis is considered benign and meningeal melanocytoma is considered relatively benign. The prognosis of meningeal

melanoma is very poor. Moreover, the prognosis of ³ patients with NCM is poor, even if the intracranial lesion is diagnosed as benign melanocytosis ^[16]. According to the literature, most patients die of benign melanocyte overgrowth or malignant transformation within 3 years after symptom onset ^[27]. In the literature, 15 patients died during follow-up (71%), the survival status of 3 patients was unknown, and 3 patients survived for a long time.

CONCLUSION

In summary, we report an adult NCM patient and summarize 21 known cases. NCM is relatively rare, especially in adult patients. Among adult patients, the proportion of male patients is higher, and most patients are found to have CMN in the trunk of the body. Therefore, patients with CMN should remain vigilant and undergo regular imaging examinations. At present, MRI is the first-choice imaging approach for diagnosing central nervous system diseases in NCM patients. Most patients develop symptoms when they are young. Although some patients may not have central nervous system symptoms until adulthood, once symptoms appear, the prognosis is poor, regardless of whether the intracranial lesions are benign or malignant. Currently, effective treatments are still lacking. Thus, more case reports describing NCM, ¹ as well as long-term follow-up studies, are warranted to fully understand NCM in the adult population. To address these limitations, our present case report provides an additional reference among the few available that can serve as a potential guide for clinicians and radiologists.

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Abdelsimar T. Omar, Marjorie Anne C. Bagnas, Krystle Anne R. Del Rosario-Blasco, Jose Danilo B. Diestro, Kathleen Joy O. Khu. "Shunt Surgery for Neurocutaneous Melanosis with Hydrocephalus: Case Report and Review of the Literature", World Neurosurgery, 2018

Crossref

77 words — 3%

3

Mian Ma, Zhi-Liang Ding, Zhi-Qi Cheng, Gang Wu, Xiao-Yu Tang, Peng Deng, Jian-Dong Wu. "Neurocutaneous Melanosis in an Adult Patient with Intracranial Primary Malignant Melanoma: Case Report and Review of the Literature", World Neurosurgery, 2018

Crossref

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4

Monika Bekiesinska-Figatowska, Orest Szczygieski, Maria Boczar, Jaroslaw Madzik et al. "Neurocutaneous melanosis in children with giant congenital melanocytic nevi", Clinical Imaging, 2014

Crossref

48 words — 2%

5

D. L. Kolin, W. R. Geddie, H. M. Ko. "CSF cytology diagnosis of NRAS-mutated primary leptomeningeal melanomatosis with neurocutaneous melanosis", Cytopathology, 2017

Crossref

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6	Striano, Pasquale, Alessandro Consales, Mariasavina Severino, Giulia Prato, Corrado Occella, Andrea Rossi, Armando Cama, Paolo Nozza, and Maria Giuseppina Baglietto. "A 3-YEAR-OLD BOY WITH DRUG-RESISTANT COMPLEX PARTIAL SEIZURES", Brain Pathology, 2012. Crossref	28 words — 1%
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