

Intracranial Intermediate-Grade Melanocytic Neoplasm: Case Report Associated with Nevus of Ota

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Abstract

Melanocytic lesions of the CNS are rare tumours originating from melanocytes that are present in the leptomeninges. They consist of a spectrum of pigmented tumours ranging from melanocytoma to melanoma. A small group of these tumours have histopathological features between those of a benign melanocytoma and a malignant melanoma; these present as intermediate grade melanocytic neoplasms. Naevus of Ota is a blue hyperpigmented dermal lesion characterized by increased number of melanocytes in the distribution of ophthalmic and maxillary divisions of the trigeminal nerve. The association of an intracranial intermediate-grade melanocytic neoplasm with a nevus of Ota is extremely rare, with only 2 cases reported in the literature to date. As a result, their behavior and progression are still poorly understood. We present the first case of a familial naevus of Ota associated with intermediate-grade melanocytic neoplasm.

Keywords

Melanocytic Neoplasm, Leptomeninges, Nevus of Ota

1. Case Report

A 50-year-old female with good past health presented to Queen Elizabeth Hospital on 7th April, 2016, with fall and left side weakness.

Upon presentation, her vitals were stable. She was fully conscious and orientated, with right side pupil measuring 4 mm and left side 3 mm. There was no deficit of other cranial nerves. She suffered from dense left hemiplegia without sensory deficit. Plain computer tomography (CT) of brain demonstrated a 4 cm right temporal hyperdense lesion with local mass effect (**Figure 1**).

Emergency craniotomy and gross total excision of the lesion were performed.

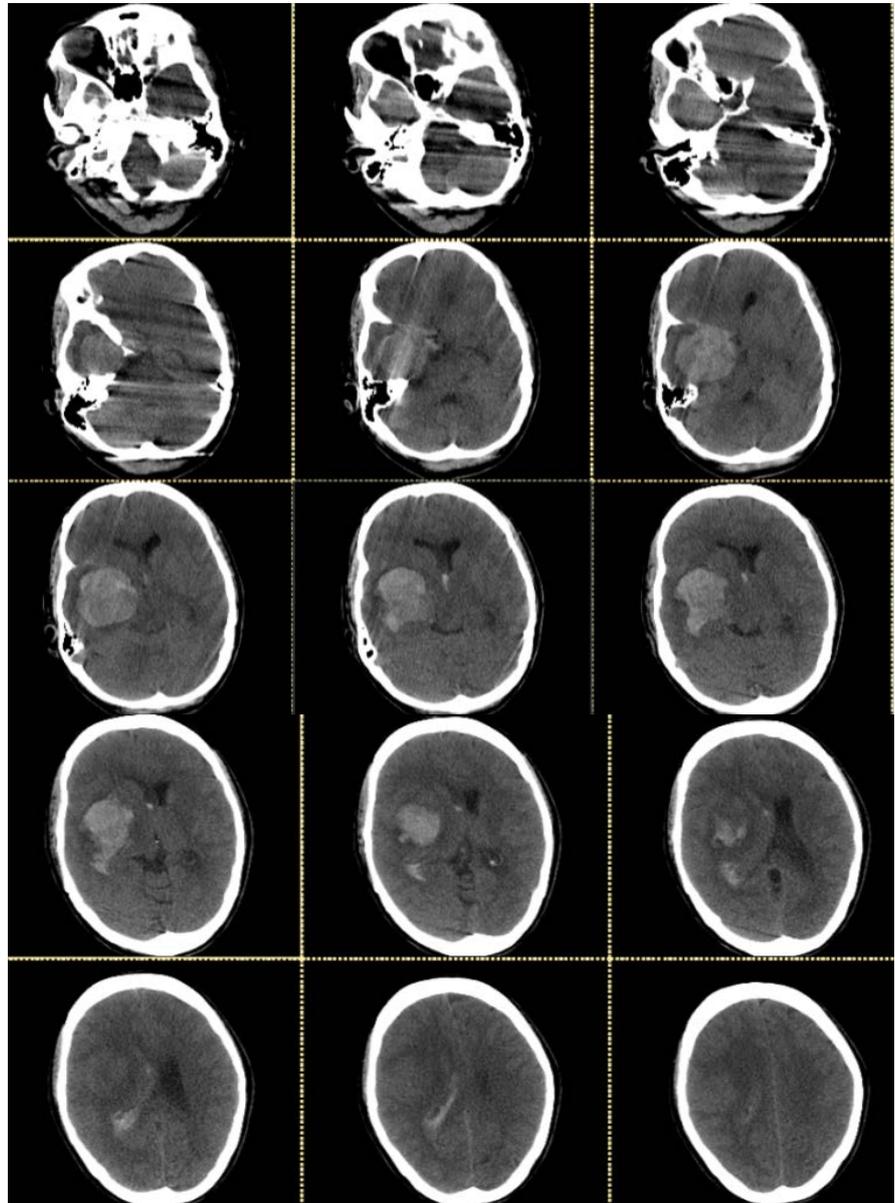


Figure 1. CT brain upon admission showing right temporal haemorrhage.

Intraoperative findings were suggestive of a pigmented lesion with haemorrhage, displacing the right internal carotid artery, right middle cerebral artery, and right third nerve.

Histopathological examination later revealed features of a melanocytic proliferation with worrisome histologic features including elevated mitosis and focal atypia, but no necrosis or anaplasia. Final pathological diagnosis was intermediate grade melanocytic neoplasm. On immunohistochemistry the tumour cells showed diffuse and strong positivity for HMB45 and patchy expression of S-100 protein. BRAF gene mutation was negative.

A detailed head-to-toe physical examination showed a left eyebrow pigmented naevus in the distribution of cranial nerve V1, which has been present without change for many years. There were no other suspicious melanocytic lesions. The

patient had no family history of melanoma.

In view of the intracranial findings, an incisional biopsy of the eyebrow lesion was performed. The final pathology was dermal dendritic melanocytosis, which can be compatible with the diagnosis of naevus of Ota.

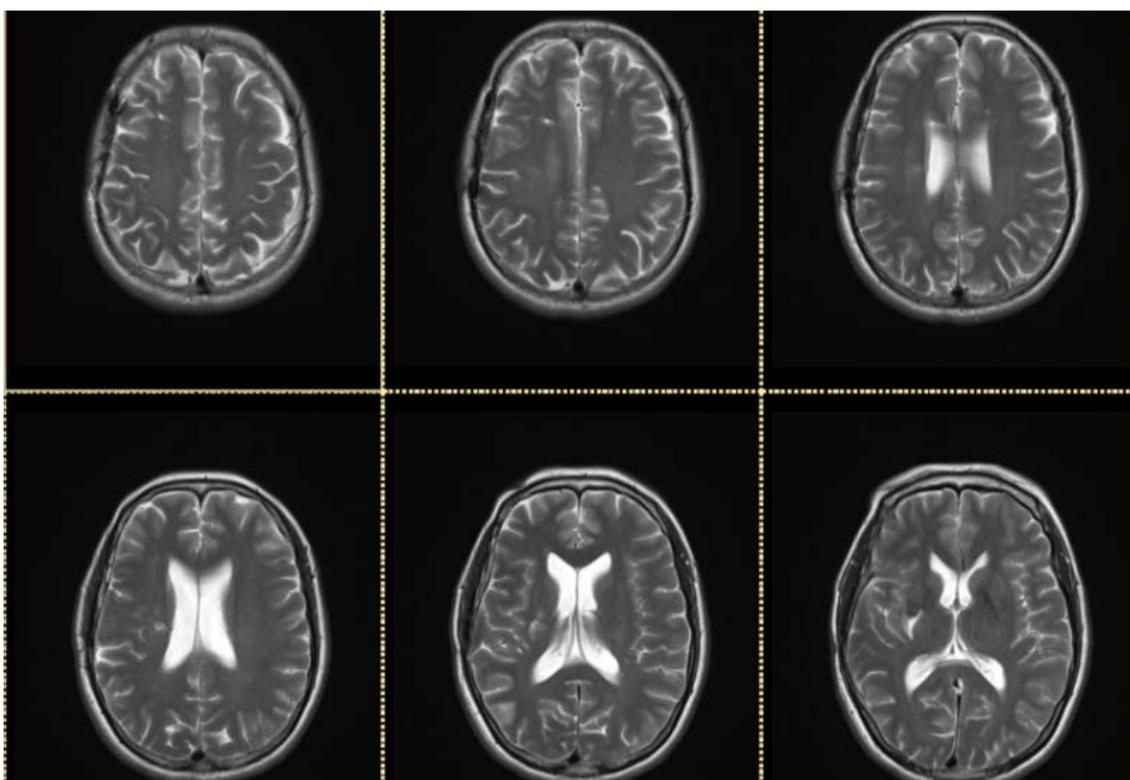
The patient further underwent whole body PET-CT and CT angiography of the brain. Both showed unremarkable findings.

Upon further questioning, the patient revealed that her 21-year-old son also has a similar left eyebrow pigmented lesion, which has been present for 3 years with no change in appearance. He had unremarkable past medical history. We performed an MRI of the brain for him, which was unremarkable.

Following the operation, the patient had transient right third nerve palsy (**Figure 2**), which spontaneously resolved at 3 months. Follow up MRI brain showed no recurrence at 4 months and 8 months after operation (**Figure 3**). Upon follow up at the outpatient clinic 8 months post operatively, she had no neurological deficit, and has returned to work full-time as a hospital janitor.



Figure 2. Patient with left naevus of Ota involving the distribution of the first (V1) branch of the trigeminal nerve. Post-operative 3rd nerve palsy is seen.



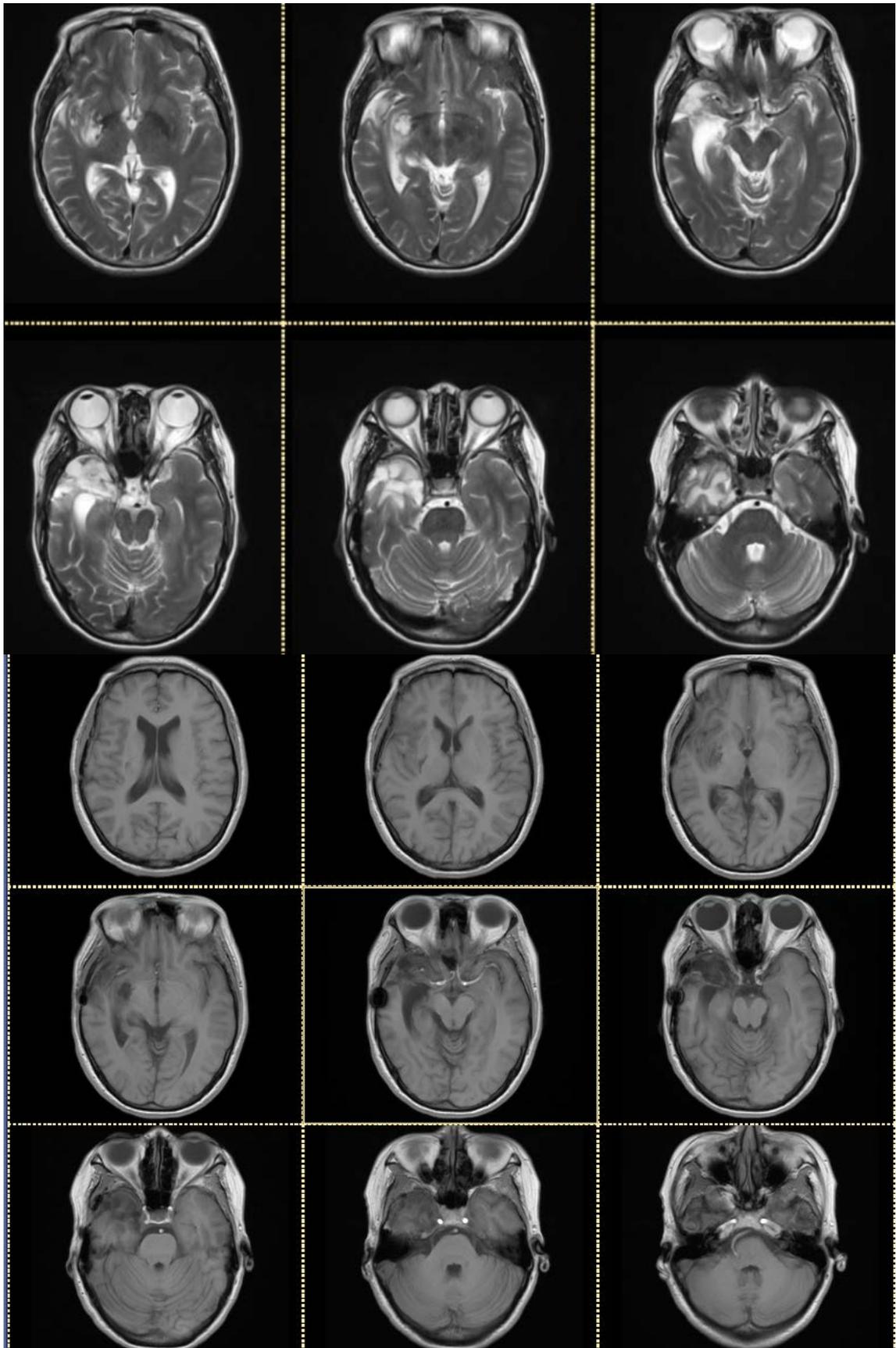


Figure 3. Follow up MRI 8 months post-operatively.

2. Discussion

Melanocytes are of neural crest in origin. Melanocytic neoplasm of the CNS associated with naevus of Ota is a rare disease. The naevus of Ota is a blue pigmented lesion that involves unilateral skin or mucous membranes in areas supplied by the trigeminal nerve [1]. It is thought to develop when migration of melanoblasts is arrested at the dermis instead of the dermoepidermal junction. It has been speculated that intracranial melanocytoma associated with the naevus of Ota both originate from melanocytes derived from the neural crest.

Primary CNS melanocytic tumours represent a spectrum of disease from well-differentiated melanocytoma to malignant melanoma. These are rare tumours with an estimated incidence 0.9 per 10 million for melanocytomas and 0.5 cases per 10 million for primary malignant melanomas [2]. They are most commonly intracranial, but can involve the spinal column, where they are most often intradural and extramedullary [3]. A small group of these tumours have histopathological features between those of a benign melanocytoma and a malignant melanoma; these are labeled as intermediate grade melanocytic neoplasm [4].

3. Literature Review

Review of the literature revealed that melanocytoma and intermediate grade melanocytic lesions can recur as malignant melanoma despite complete excision [5] [6]. This supports the previously proposed theory of melanocytoma, intermediate grade melanocytic neoplasm, and malignant melanoma as a continuous spectrum of disease, rather than each being a separate disease entity. With this knowledge, it is important to review these three diagnoses in conjunction with a naevus of Ota.

Literature search via Pubmed and EMBASE revealed 11 previous cases of melanocytoma and 2 cases of intermediate grade melanocytic neoplasm to date, and at least 11 cases of melanoma have been reported in conjunction with naevus of Ota (Table 1).

All reported cases of melanocytoma were ipsilateral to the naevus of Ota, where occasionally intermediate grade melanocytic neoplasms and melanoma have been found to occur contralateral to the cutaneous lesion. The reason for this is still largely unknown. We hypothesize that intracranial lesions that develop contralateral to the naevus of Ota may represent a more aggressive lesion and a different disease entity with higher risks of malignant transformation.

Management and outcome

Literature search showed that treatment options for patients with melanocytoma, intermediate grade melanocytic neoplasms, and melanomas were heterogeneous, with no established consensus. In most cases, patients underwent surgical excision, with a few cases also receiving radiotherapy or chemotherapy.

There have been few publications on the treatment of these neoplasms. Rades and colleagues published one of the more substantiated studies in 2004. The retrospective review of 89 meningeal melanocytomas showed that the five-year-survival rate was 100% in patients who received complete resection, but only

Table 1. (a) Melanocytoma occurring in conjunction with a naevus of Ota, (b) Intermediate grade melanocytic neoplasm occurring in conjunction with a naevus of Ota, (c) Malignant melanoma occurring in conjunction with a naevus of Ota.

(a)							
Author/Year	Age/sex	Naevus of Ota	Site of intracranial lesion	Presenting symptoms	Excision	RT/chemo	Outcome
Botticelli 1983 [7]	43/F	Left	Leftmeckel's cave.	Left CN4 palsy, left ptosis, enophthalmos	Total	Yes/No	Recur 2 years later, subtotal excision + RT. No more recurrence
Moon WS 1992 [8]	53/M	Right	Right parietooccipital, left frontal	Right hemiparesis, vomiting	Total	No/No	Recurred
Piercecchi-Marti 2002 [9]	25/M	Right	Right frontoparietal	Strabismus, headache, grandma seizure	Total	No/No	No recurrence
Rahimi 2003 [10]	17/M	Left	Left parietal	Headache, blindness	Total	No/No	N/A
Rutten 2005 [11]	37/F	Right	Right olfactory groove	Headache, loss visual acuity	Total	No/No	Multifocal recurrence, total excision → RT. No more recurrence
Hino K 2005 [12]	75/F	Right	Right anterior clinoid process, intraorbital	Decreased vision, disturbed consciousness	Partial	No/No	No recurrence (but apallic state)
Hao Pan 2011 [13]	36/M	Right	Right cavernous sinus	Headache, ptosis	Subtotal	Yes/No	No recurrence
Wu C 2011 [14]	36/M	Right	Right cavernous sinus	N/A	Total	No/No	N/A
Munoz-hidalgo 2014 [15]	15/M	Right	Right temporal	Headache, vomiting	Total	No/No	No recurrence
Hongxu Chen 2015 [16]	20/F	Left	Left cerebellar hemisphere	Headache	Total	No/No	N/A
Mohammad Samadian 2015 [17]	19/M	Left	Left temporal	Seizure	Total	No/No	No recurrence
(b)							
Author/Year	Age/sex	Naevus of Ota	Site of intracranial lesion	Presenting symptoms	Excision	RT/chemo	Outcome
Marta Navas 2009 [18]	25/M	Right	Right temporal	Right CN3 palsy	Total	No/No	Died post-op due to malignant infarct of right hemisphere
Shin 2015 [19]	56/F	Right	Left temporal	Headache, confusion	Total	Yes/No	No recurrence
(c)							
Author/Year	Age/sex	Naevus of Ota	Site of intracranial lesion	Presenting symptoms	Excision	RT/chemo	Outcome
Enriquez 1973 [20]	43/M	N/A	Pineal, meningeal	N/A	No	No/No	Death
Sang DN 1977 [21]	58/M	Left	Right frontal	Headache, incontinence, left CN7 palsy	No	Yes/No	Mass similar with no progression 6 months later
Horseley 1980 [22]	37/F	Left	Left parietal, left temporal bone	Headache, CN6 palsy, nausea, vomiting	Total (parietal)	Yes/No	No recurrence
Sagar HJ 1983 [23]	23/F	Right	Right temporal	Partial seizure	Total	No/No	No recurrence
Kubato 1988 [24]	77/M	Left	Left temporal	Disturbed consciousness, left hemiparesis	Subtotal	No/Yes	Death 3 weeks post op
Hartmann LC 1989 [25]	41/F	Right	Right middle fossa	Headache	Total	No/No	Recur 6 months later. Observe. FU 1 year post op unchanged
Johnson RR 1999 [26]	42/M	Left	Left occipital	Headache, right upper quadrantonopia, scotoma	Subtotal	Yes/No	Static residual mass 3 months post-op
Azar 2010 [27]	21/M	Left	Right parietal, right retrobulbar, right cavernous sinus	Left hemiparesis + headache	Total (parietal)	Yes/Yes	Melanoma dissemination

Continued

Wang J 2013 [28]	52/F	Left	Left temporal	Recurrence of previous melanoma on MRI (16 months post-op)	Total	No/No	No recurrence
Wang J 2013 [28]	33/F	Left	Left tentorium cerebelli	Headache, left facial numbness	Total	No/No	No recurrence
Bharat Guthikonda 2015 [29]	32/F	Left	Right frontotemporal	Left side numbness	Total	No/No	N/A

46% in those whose resection was incomplete. However, the survival rate improved to 100% in patients with incomplete resection and adjunct radiation therapy. Based on this, they concluded that complete tumor resection is the best therapeutic option, and in cases of incomplete resection, radiotherapy should be considered [30].

A retrospective review published by Rodriguez Y in 1992 on 81 cases of primary solitary intracranial melanoma also showed similar improved survival (19.6 ± 2.3 months) in patients with complete removal of the tumour than patients undergoing partial removal or biopsy (9.3 ± 2.4 months). Patients who were not operated had a shorter survival than both surgical subgroups of patients [31].

Unfortunately, based on the above literature review, follow up data for patients with naevus of Ota and CNS melanocytic neoplasm is lacking and heterogeneous. However, from the limited evidence available, we can conclude that recurrence and even metastasis of the previously thought to be benign melanocytoma is not uncommon. Therefore, follow up with regular imaging is important.

4. Conclusions

Primary CNS intermediate grade melanocytic neoplasm and concomitant nevus of Ota have been rarely reported. This is the third reported case in literature so far. It is made more unique due to the fact that this is the first reported case in which a familial naevus of Ota occurs together with an intracranial melanocytic lesion.

There is no standard treatment protocol for intermediate grade melanocytic neoplasm occurring simultaneously with a Nevus of Ota. Based on data extrapolated from treatment for meningeal melanocytoma and primary intracranial melanoma, we propose that complete surgical excision should be considered as the best therapeutic option. Close monitoring with imaging of patients with intermediate grade melanocytic neoplasm post-operatively is important.

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