ORIGINAL SCIENTIFIC ARTICLES

Intracranial Colloid Cyst in a Young Female with Neurofibromatosis Type 1: A Case Report

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ABSTRACT

Introduction

Intracranial colloid cysts are rare benign tumors located in the region around the foramen of Monro or around the third ventricle with an annual incidence of 3 of 1,000,000. The common clinical picture is a progressive headache due to the rapid enlargement of the cyst, resulting in hydrocephalus as it obstructs the cerebrospinal flow; brain herniation may ensue, leading to death.

Objectives

The objectives of this report are to (1) present a case of intracranial colloid cyst in a young female with neurofibromatosis type 1, (2) emphasize the importance of early diagnosis by clinical signs and symptoms and (3) highlight the importance of neuroimaging in arriving at a neurologic diagnosis.

Case Report

A nineteen-year-old female was seen due to a three-month history of progressive headache, with associated signs of increased intracranial pressure and with a medical history of neurofibromatosis type 1, inherited from her mother. Neurologic findings revealed papilledema and 6th cranial nerve palsy. By radiographic imaging with clinical correlation, patient was diagnosed with a colloid cyst obstructing the foramen of Monro. Surgical intervention was done and patient improved without complications.

Discussion

Neurofibromatosis is a hereditary neurocutaneous syndrome in which the skin, nervous system, bones, endocrine glands and sometimes other organs are the sites of a variety of congenital abnormalities, often taking the form of benign tumors. Intracranial colloid cyst was seen in this case report. Colloid cysts have an incidence of 0.5 – 1% of all primary brain tumors and are the most common masses in the third ventricle and in the Foramen of Monro. They cause obstruction of CSF flow, resulting in hydrocephalus. No published case of neurofibromatosis type 1 patients with a symptomatic intracranial colloid cyst has been reported yet. Surgical resection is the treatment of choice for colloid cyst.

Keywords: *intracranial colloid cyst, neurofibromatosis type 1, headaches, hydrocephalus*

INTRODUCTION

Intracranial colloid cysts are rare benign tumors located in the region around the Foramen of Monro or in the anterosuperior portion of the third ventricle having an annual incidence of 3 of 1,000,000 [1,2]. Common clinical picture is a progressive headache due to the rapid enlargement of the cyst, resulting in hydrocephalus as it obstructs the cerebrospinal flow, and brain herniation may ensue leading to death[3]. Age of onset

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peaks at the third to fourth decade of life and is rare in children[4]. This case report presents a nineteen-year-old female with neurofibromatosis type 1, presenting with progressive headache and signs of increased intracranial pressure. Cranial MRI with contrast revealed a third ventricular colloid cyst with hydrocephalus. A thorough case search was done using PubMed and Google Scholar for case reports of intracranial colloid cysts in neurofibromatosis type 1. To the knowledge of the author, only one study was published wherein 53 patients with neurofibromatosis type 1, only one patient had an asymptomatic colloid cyst[5], in comparison with this case report of a symptomatic colloid cyst.

OBJECTIVES

The objectives of this report are to (1) present a case of intracranial colloid cyst in a young female with neurofibromatosis type 1, (2) emphasize the importance of early diagnosis by clinical signs and symptoms and (3) highlight the importance of neuroimaging in arriving at a neurologic diagnosis.

CASE PRESENTATION

A nineteen-year-old right-handed female was referred to the Neurology Outpatient Department due to a three-month history of progressive headaches. Headaches were characterized as intermittent, mild, throbbing, 3-4/10 in intensity, localized at bilateral parieto-temporal areas and occurring upon waking up; pain was relieved with activity and intake of analgesics. The headaches progressed to a severe intensity with associated diplopia and vomiting. She was noted to have increased sleeping time by family members prompting admission.

On physical examination, there were multiple café au lait spots on her trunk and extremities (Figures 1A and 1B) and with soft non-tender nodules on bony prominences (Figure 2). Freckles were noted on both axillary areas (Crowe's sign), and Lisch nodules on both irises. Other physical findings were unremarkable.

Upon neurological examination, the patient had intact higher cortical functions with a mini mental status score of 30/30 (normal). On gaze examination, her left eye was esotropic with a left lateral rectus palsy (Figure 3). Funduscopy revealed grade 3 papilledema. There were no associated lateralizing weakness, sensory deficits and other long tract signs. Tests for meningeal irritation were unremarkable.

Skin biopsy of a nodule on her left shoulder was consistent with a neurofibroma. Surgical intervention by craniotomy via transcallosal approach with ventriculo-peritoneal shunting was done. Biopsy and excision of the intracranial mass, however, showed glial tissues with focal hemorrhages and reactive gliosis. Post-operative state was unremarkable, and the patient was eventually discharged improved.

She was seen in the outpatient department one week after hospital discharge. Patient came in ambulatory, with no headaches although she still had a left lateral rectus palsy. On succeeding follow ups, there was gradual disappearance of her left lateral rectus palsy and the rest of her neurologic examination was unremarkable.

DISCUSSION

Neurofibromatosis is a hereditary neurocutaneous syndrome in which the skin, nervous system, bones, endocrine glands, and sometimes other organs are the sites of a variety of congenital abnormalities, often taking the form of benign tumors[6]. Prevalence of this was reported to be 30 to 40 per 100,000, with the expectancy of 1 case in every 2,500 to 3,300 births[6,7,8]. This neurocutaneous disorder is autosomal dominant with approximately 50% of cases classified as sporadic and 50% familial[6,8]. Diagnosis of neurofibromatosis is clinical, with a diagnostic criterion (Table 1). Fulfilling two of the seven criteria warrants diagnosis of neurofibromatosis type 1 (NF1). Our patient

Figure 1A. Upper back, abdomen and left arm respectively showing café-au lait spots patches*

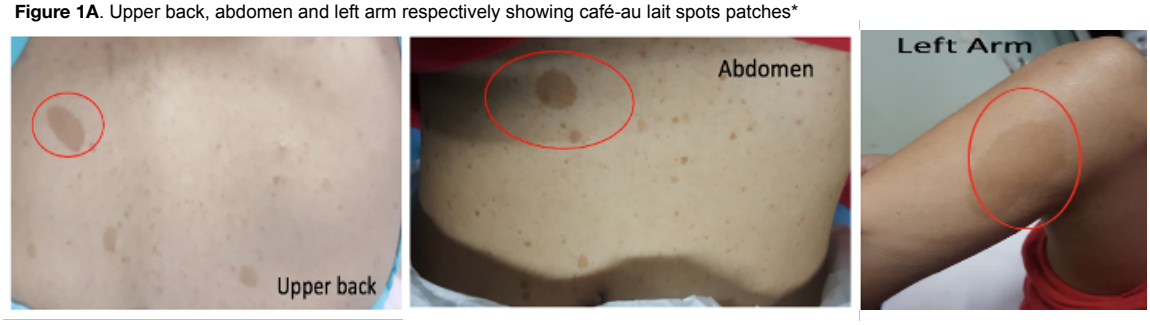


Figure 1B. Largest café-au lait spot measuring 9 cm x 4cm.

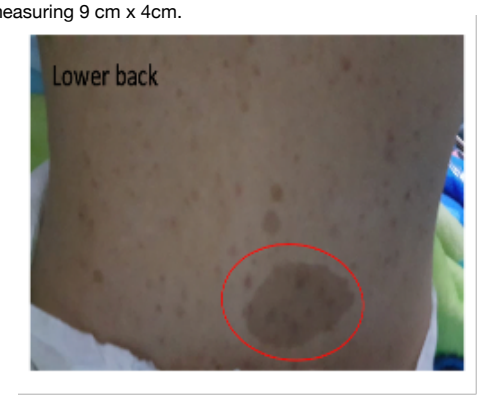


Figure 2. Neurofibromas present on different extremities.

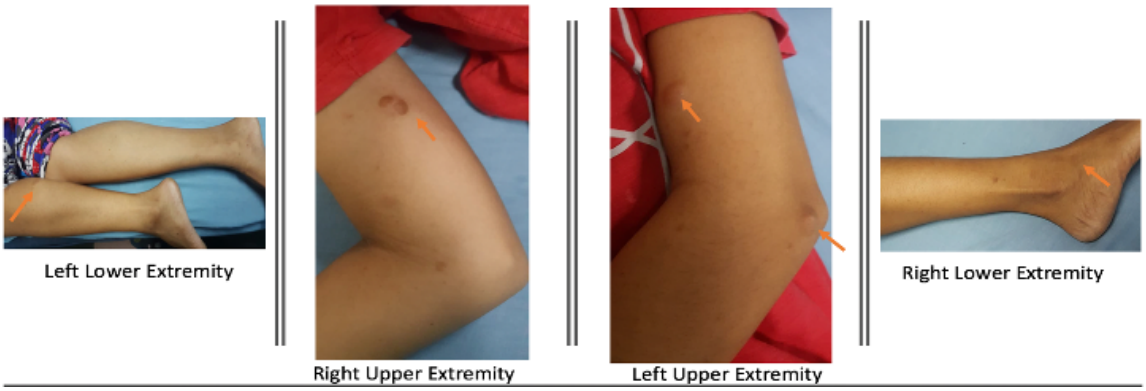
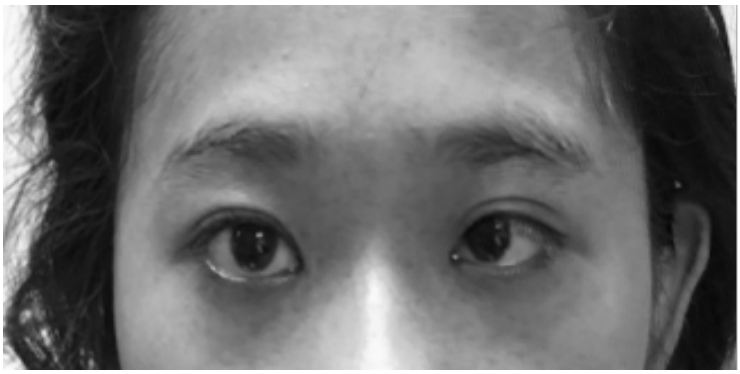


Figure 3. Lateral rectus palsy of left eye, with left eye esotropia on primary gaze.



*Images presented were taken with patient and parental consent. Images are permitted by the patient and her family to be used for publishing of this case report.

Figure 4A. Cranial MRI contrast study T1 showing a round isointense mass lesion at the foramen of Monro measuring 1.1x1.5x1.1cm which is barely visible, and dilatation of third ventricle and lateral ventricles.

Figure 4B. Cranial MRI contrast study T2 showing a round isointense mass lesion with the same characteristic as in Figure 4A.

Figure 4C. Cranial MRI contrast study, FLAIR showing hyperintense mass lesion with the same characteristic in Figure 4A.

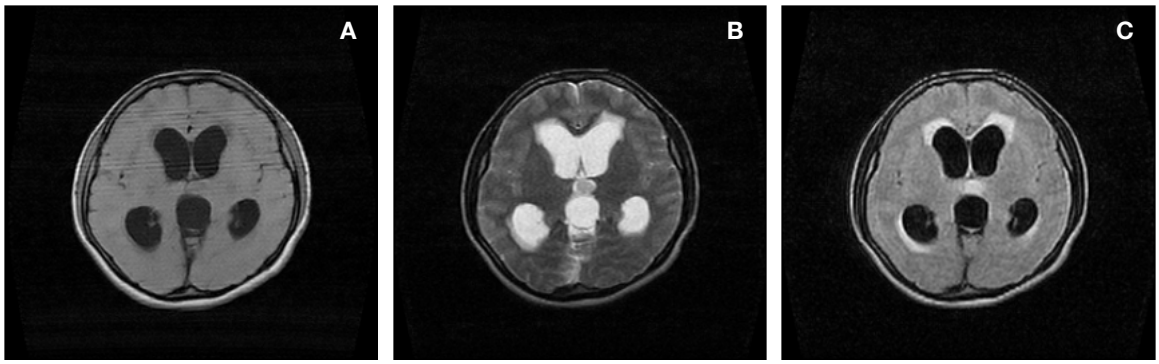


Figure 5. Mother with characteristic neurofibroma lesions in the face.

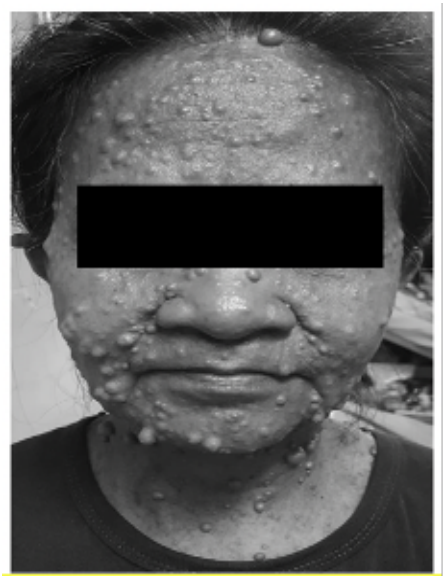
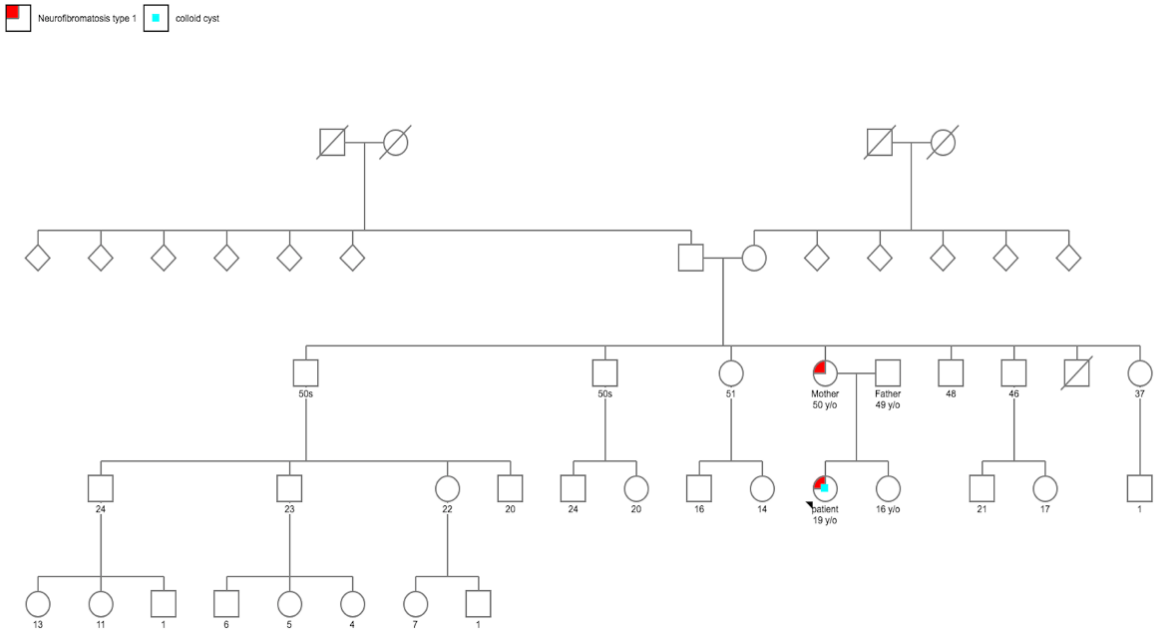


Table 1: Diagnostic criteria for neurofibromatosis 1 (NF1) (NIH consensus development conference 1988)

6 or more café au lait macules (0.5 cm in children or 1.5 cm in adults)
2 or more cutaneous/subcutaneous neurofibromas or one plexiform neurofibroma
Axillary or groin freckling
Optic pathway glioma
2 or more Lisch nodules (iris hamartomas seen on slit lamp examination)
Bony dysplasia (sphenoid wing dysplasia, bowing of long bone pseudarthrosis)
First degree relative with NF1

Illustration 1. Family genogram of patient's maternal side. Neurofibromatosis type 1 present only with patient and her mother. Boxes represent males, circles represent females, diamond figures are of unknown sex, and crossed out figures as deceased



manifested five out of seven clinical signs and symptoms, (café au lait macules, neurofibroma, axillary freckling, Lisch nodules and first-degree relative with NF1) arriving at the diagnosis of neurofibromatosis type 1. Her mother has similar cutaneous lesions (Figure 5), and a genogram (Illustration 1) describes her mother's condition as sporadic. Along with these clinical signs and symptoms, there are other associated conditions such as cardiac malformations, cardiovascular diseases, vasculopathy, hypertension, vitamin D deficiency, brain malformations and seizures [7,9]. Interestingly, there were no such associated conditions seen in our case.

RASopathies are genetic diseases causing germline mutations that encode or regulate the Ras/mitogen-activated protein kinase (MAPK) pathway, responsible in regulation of cell cycle, cellular growth and differentiation. Examples of which are neurofibromatosis type 1, Noonan syndrome, Noonan syndrome with multiple lentigines, capillary malformation–arteriovenous malformation syndrome, Costello syndrome, cardio-facio-cutaneous syndrome, and Legius syndrome[9]. Neurofibromatosis type 1 is caused by mutations in the NF1 gene, located in chromosome 17q11.2 that encodes the protein neurofibromin. Neurofibromin is expressed in neuronal (oligodendrocytes, Schwann cells) and non-neuronal tissues. Neurofibromin mutations reduces RasGTPase activity, increasing GTP bound RAS thus increasing cell proliferation and differentiation[7, 9]. Heterozygous loss of NF1 appears to affect actin cytoskeleton motility, pointing to cellular dysfunction; irregular shapes, adhesion and invasiveness which are key factors for tumorigenesis[7].

Individuals with NF1 are at greater risk of developing malignancies, especially in pediatric populations. Examples of which are optic pathway gliomas, rhabdomyosarcoma, neuroblastoma and juvenile myelomonocytic leukemia. In adults, malignancies reported were peripheral nerve sheath tumors, gastrointestinal stromal tumors, somatostatinomas, pheochromocytomas and breast carcinomas[7,9]. Optic gliomas are the most common type of brain tumor associated with this disease affecting 15-20% of individuals, specifically located in the optic pathway, brainstem and cerebellum[7,8,9]. For this case, an enlarging intracranial mass with

a radiographic diagnosis of colloid cyst was seen by magnetic resonance imaging, obstructing the flow of cerebrospinal fluid in the third ventricle (Figure 4).

Colloid cysts, although rare (seen in 0.5 – 1% of all primary brain tumors[2]), are a strong and practical diagnosis for this case, as it is the most common mass in the third ventricle. This was also associated with obstructive lesions in the Foramen of Monro, resulting in hydrocephalus[2,4,12]. Even without a biopsy report, it is safe to conclude a diagnosis based on clinical presentation and radiographic findings[1,2,3,4,13]. Ninety percent of colloid cysts are asymptomatic and stable. Most of them are incidental findings post-mortem, with 10% of reported cases leading to brain herniation and death[12]. A similar case was reported with death as an outcome in a young woman with similar signs and symptoms, due to rapid enlargement of the colloid cyst[3], making the immediate diagnosis and management of these cases even more urgent and controversial. Demographics in particular show equal distribution among males and females[4], but in the literature, most of the reported symptomatic cases were women[2,10].

Magnetic resonance imaging of colloid cysts are variable due to cyst ingredients, particularly cholesterol and hemorrhagic contents[1]. MRI T1W signal correlates cholesterol concentration, 2/3 are hyperintense and 1/3 are isointense, with associated ventriculomegaly. T2W signals are more variable as it reflects water content, with majority as isointense[4]. Although MRI features are variable, colloid cysts could be isointense, hypointense or hyperintense on T1W, with cyst wall showing non-enhancement in contrast studies[16]. MRI imaging of our case coincides in the 1/3 aspect of MRI findings, indicating a non-cholesterol containing cyst.

Surgical resection is the treatment of choice for colloid cyst[4,10]. In our case, endoscopic surgical approach was first done; but with difficulty due to the deep location of the third ventricle in the middle of the brain parenchyma, transcallosal approach was performed instead. Complete excision was not done. Either craniotomy or endoscopic approaches may be done, as only the removal of the cyst or its fenestration will improve CSF flow and its symptoms[13]. Such surgical approaches are difficult in these situations, as the third ventricle is a deep midline structure, with adjacent vital organs such as the hypothalamus[14]. It is known that incomplete resection carries a higher risk of recurrence [13,14], but both endoscopic approach and craniotomy with microsurgical resection are equal in mortality and shunt dependency[15]. Contents of colloid cysts in biopsies are variable, with mucin and colloid as the most common; the presence of cholesterol, cellular debris and hemorrhage within the cyst have also been reported[10,16]. Grossly, it is a unilocular round structure filled with viscous material, with the cell wall as a thin columnar epithelium, and with cyst contents of desquamated ghost cells and filamentous materials[17]. In our case, biopsy of the cyst showed a neurological tissue with focal hemorrhage and reactive gliosis which may not be representative of the mass, as reported by the pathology department.

CONCLUSION

Neurologists should be cautious and vigilant in dealing with first episode headaches, especially if accompanied with signs of increased intracranial pressure. Immediate neuroimaging is warranted in such cases. A thorough neurologic and physical examination of patients is necessary to avoid misdiagnosis. A delay in treatment strategy may lead to neurologic deterioration, poor outcome and increased mortality rates.

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