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Pathogenesis of Intracranial Lipoma: An MR Study in 42 Patients

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Intracranial lipomas are uncommon lesions whose development remains poorly understood. To clarify the anatomic and embryologic features of intracranial lipomas, we retrospectively reviewed the MR scans of 42 patients with 44 intracranial lipomas. Interhemispheric lipomas were the most common, accounting for 45% of cases. The remainder of the lesions were clustered in the quadrigeminal/superior cerebellar (25%), suprasellar/interpeduncular (14%), cerebellopontine angle (9%), and sylvian (5%) cisterns. Fifty-five percent of the lesions were associated with brain malformations of varying degrees. Intracranial vessels and nerves were noted to course through 16 (36%) of the lesions.

The relative frequencies of the locations of the lipomas correspond to the temporal sequence of dissolution of the meninx primitiva, the mesenchymal anlage of the meninges. This finding supports the concept of lipoma formation as a result of abnormal persistence and maldifferentiation of the meninx. This embryologic concept of the development of intracranial lipomas explains the high frequency of callosal and other brain hypoplasias. Intracranial lipomas are neither hamartomas nor true neoplasms; rather, they are congenital malformations.

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The intracranial lipoma, which has traditionally been considered little more than a curiosity by radiologists, has inspired numerous pathogenetic theories. It has been described in dysraphic terms as a mesodermal inclusion within the closing neural tube [1, 2]; in hyperplastic terms as a proliferation of fat cells normally present within the leptomeninx [1, 2]; in metabolic terms as the deposition of fatty, catabolic products of nerve tissue [2, 3]; and in heterotopic terms as the surviving derivative of a displaced dermal anlage in which other mesenchymal elements recede [2, 3]. Another theory [4, 5] attempts to address the congenital, malformative nature of intracranial lipomas. This concept, proposed by Verga [4], holds that intracranial lipomas derive from the embryologic "meninx primitiva" described by Salvi [6]. Although initially thought to be of mesodermal origin, it is now clear that the meninx primitiva is a mesenchymal derivative of neural crest [6, 7]. Normally the inner meninx is resorbed by an orderly process, as its extracellular space expands to create the subarachnoid cisterns.

While reviewing a large number of intracranial lipomas, it became apparent that these lesions occur in consistent locations and are associated with specific brain malformations. Furthermore, it became apparent that the theory of Verga and its refinements, although fundamentally correct, fail to address the reason that intracranial lipomas consistently occur in the same locations. We believe this question can now be satisfactorily answered. The purpose of this article is to review the MR imaging characteristics, the anatomic distribution, and the numerous pathogenetic theories regarding intracranial lipomas. With this information, we hope to unify the original concept of Verga of a malformative origin with more recent data in an attempt to clarify the etiology of intracranial lipomas.

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Materials and Methods

The MR scans of 42 patients with 44 intracranial lipomas were reviewed retrospectively. The patients ranged in age from prenatal to 82 years old. Thirty-six scans were obtained at 1.5 T and six were obtained at 0.3–0.5 T. The lesions were evaluated relative to location, the presence of other (related or unrelated) congenital brain anomalies (such as hypothalamic/mamillary body and corpus callosal hypoplasia), the identification of a chemical-shift artifact (CSA), and the presence or absence of vessels within the lipomas. Pericallosal* lipomas were also assessed for extension along the choroidal fissures. Sagittal, axial, and coronal spin-echo (SE) images, 477–800/15–40/1–4 and 2300–3000/30–120/1–2 (TR/TE/excitations), were reviewed. Various matrix sizes (128–256 × 256) and slice thicknesses (3–5 mm) were used, depending on the magnetic field strength, indication for scanning, and patient age. Fat saturation techniques were used in three cases at 1.5 T.

Results

All lesions were identified by marked hyperintensity on short TR images and characterized as fat by progressive diminution of signal intensity with increased T2 weighting. As seen in Table 1, the lipomas were distributed within the subarachnoid cisterns and spaces as follows: pericallosal (16); quadrigeminal/superior cerebellar (11); sylvian (two); suprasellar (five); interpeduncular (one); cerebellopontine angle (CPA) (three); velum interpositum (two); and anterior interhemispheric fissure, cistern of the lamina terminalis, internal auditory canal (IAC), and prepontine cistern (one each).

Of the 16 pericallosal lesions, 11 anteriorly situated, bulky lipomas were associated with either agenesis (three) or severe hypogenesis (eight) of the corpus callosum (Fig. 1). Vascular flow void within the lipoma, representing either an azygous anterior cerebral artery (ACA) or both ACAs, was noted in all 11 bulky pericallosal lipomas. Lipomas within the lateral ventricular choroid plexuses were detected in eight of the 11. Of the eight, contiguous extension from the parent lesion through the choroidal fissures was easily seen in six; in two cases the images were inadequate to assess the choroidal fissures. One lesion was associated with a frontonasal encephalocele and callosal agenesis, although the lipoma did not extend into the encephalocele.

Five pericallosal lipomas appeared on short TR images either as a ribbon of high intensity along the dorsum of the corpus callosum with posterior extension around the splenium (Fig. 2) or as a retrosplenial button of fat. Mild callosal hypoplasia was seen in all five cases. The splenium was hypoplastic in two, the posterior body of the corpus callosum was foreshortened in two, and a dorsal groove in the corpus callosum was seen in one ribbonlike pericallosal lipoma. Two of these five pericallosal lesions demonstrated contiguous choroidal extension, and ACA flow void was detected within the lipoma in only one of the five cases. One of the two lipomas of the cistern of the velum interpositum was associated with choroidal extension on the right, and also demonstrated intralipoma flow void. The other extended posteriorly around the splenium (Fig. 3).

Eleven lipomas were detected within the quadrigeminal and/or superior cerebellar cisterns (Figs. 4 and 5). All were adjacent to the inferior colliculus, superior medullary velum, and/or superior vermis. Hypoplasia of either one inferior colliculus or the superior vermis was clearly evident in four cases. Hydrocephalus, secondary to aqueductal stenosis, was present in one case. Two of the 11 cases were pathologically proved to be benign, mature lipomas.

Five lipomas were detected in the suprasellar cistern and hypothalamus (Fig. 6). Three were intimately related to the mamillary bodies, which were small in one case. Images in the other two cases were inadequate to assess the mamillary bodies. Two lipomas were situated adjacent to and possibly partially within the tuber cinereum.

Three lipomas were situated within the CPA cistern; another was predominantly in the internal auditory meatus, with a small CPA cisternal component. The intracanalicular neural elements coursed through the substance of the IAC lipoma. Similarly, the seventh/eighth cranial nerve complex was noted within the substance of one of the CPA lipomas, both on MR and at surgery (Fig. 7).

One lipoma was detected within the cistern of the lamina terminalis and was associated with agenesis of the corpus callosum as well as a sphenoid encephalocele. The lipoma did not extend into the encephalocele. Two lipomas were detected within the sylvian fissure; in one of these flow void related to middle cerebral artery branches was demonstrated. Both were in patients with bulky pericallosal lipomas. One of the lesions was pathologically proved and has been reported previously [8]. The final lesions included an interpeduncular lipoma (accompanied by a second lesion adjacent to the mamillary bodies) and a surgically proved prepontine lipoma associated with pontine hypoplasia (Fig. 8).

CSA was appreciated on 29 (69%) of the 42 MR studies, including two (33%) of the six at mid field strength and 27 (75%) of the 36 at high field strength. The lipomas that did not exhibit CSAs at mid field strength included a ribbonlike pericallosal lesion and a lipoma of the quadrigeminal/superior cerebellar cistern, which was greater than 2 cm in diameter. The lipomas that did not demonstrate CSAs at 1.5 T were all less than 1 cm in diameter, with the exception of the two lipomas of the cistern of the velum interpositum (1.8 cm).

Thus, of the 40 lipomas for which images were adequate to assess the adjacent brain, 24 (60%) were associated with radiographically detectable congenital anomalies of the adjacent neural tissue. In two others, the seventh and/or eighth cranial nerve complex was detected within the lipoma. All pericallosal lipomas were associated with either callosal agenesis or some degree of callosal hypogenesis.

Discussion

The earliest reported intracranial lipoma appears to date back to 1818, when Meckel described a chiasmatic lipoma.*

* Although semantically inaccurate, interhemispheric lipomas are more commonly known as either lipomas of the corpus callosum or pericallosal lipomas even when the corpus callosum is absent. For the sake of continuity, we will use the term *pericallosal lipoma*.

* Verga [4], in 1929, referenced Wenzel's case report of 1812, which described a "lipoma" of the olfactory tract. This, however, was disputed by Krainer [5] in 1935, who argued that Wenzel's case actually represented a cholesteatoma.

TABLE 1: MR Characteristics of Intracranial Lipomas

Magnetic Field Strength/Case No.	Lesion Location, Type	CSA	Flow Void	Other Brain Anomalies	Choroidal Extension
0.3–0.5 T ^a					
1	Ant pericallosal, bulky	Yes	Yes	Hypoplasia of CC; SP absent	Bilateral
2	Pericallosal, ribbonlike	Yes	No	Dorsal groove, CC	R, from below
3	Pericallosal, ribbonlike	No	No	Mild hypoplasia of CC, CSP, CV	No
4	L CPA	No	No	No	–
5	Sup cerebellar ^b	No	No	No	–
6	Sup cerebellar ^b	No	No	Mild hypoplasia of left inferior colliculus	–
1.5 T					
7	Ant pericallosal, bulky	Yes	Yes	Hypoplasia of CC	Bilateral, contiguous
8	Ant pericallosal, bulky	Yes	Yes	Hypoplasia of CC	Bilateral, contiguous
9	Ant pericallosal, bulky	Yes	Yes	Hypoplasia of CC	Bilateral, contiguous
10	Ant pericallosal, bulky	Yes	Yes	Hypoplasia of CC	Inadequate images
11	Ant pericallosal, bulky	Yes	Yes	Agenesis of CC, SP	Bilateral, contiguous
12	Ant pericallosal, bulky	Yes	Yes	Hypoplasia of CC	No
13	Ant pericallosal, bulky ^c	Yes	Yes	Hypoplasia of CC	Bilateral, contiguous
14	Ant pericallosal, bulky L sylvian	Yes	Yes	Agenesis of CC, SP	Bilateral, not contiguous
		No	No	No	No
15	Ant pericallosal, bulky R sylvian ^b	Yes	Yes	Hypoplasia of CC	Bilateral, contiguous
		Yes	Yes	No	–
16	Ant pericallosal, bulky	Yes	Yes	Agenesis of CC, SP; craniofacial dysplasia; frontonasal encephalocele	No
17	Pericallosal buttonlike	Yes	No	Hypoplasia of splenium	No
18	Pericallosal, ribbonlike	Yes	Yes	Hypoplasia of CC	No
19	Pericallosal, ribbonlike	Yes	No	Hypoplasia of splenium, CSP	Bilateral, contiguous
20	Interhemispheric	Yes	No	No	No
21	Velum interpositum	No	Yes	No	R, not contiguous
22	Velum interpositum	No	No	No	No
23	Sup cerebellar	Yes	No	Mild hypoplasia, Sup vermis	–
24	Sup cerebellar	Yes	No	No	–
25	Sup cerebellar	Yes ^c	No	Mild hypoplasia, Sup vermis	–
26	Sup cerebellar	No	No	No	–
27	Sup cerebellar	No	No	No	–
28	Quadrigeminal	No	No	No	–
29	Quadrigeminal	Yes	No	Hypoplasia, R inferior colliculus	–
30	Quadrigeminal	Yes	No	Hypoplasia, R inferior colliculus; aqueductal stenosis	–
31	Quadrigeminal	No	No	No	–
32	Suprasellar (mamillary body)	Yes	No	Hypoplasia of hypothalamus/mamillary bodies	–
33	Suprasellar (mamillary body)	Yes	No	Inadequate images	–
34	Suprasellar (mamillary body)	Yes	No	Inadequate images	–
35	Suprasellar (tuber cinereum)	No	No	No	–
36	Suprasellar (tuber cinereum)	Yes	No	Inadequate images	–
37	Interpeduncular (second mamillary body component)	Yes	No	Inadequate images	–
38	R CPA ^b	Yes	Yes ^d	No	–
39	L CPA	Yes	No	No	–
40	L IAC	No	Yes ^d	No	–
41	Lamina terminalis	No	No	Agenesis of CC, SP; sphenoid encephalocele	–
42	Prepontine ^b	No ^c	No	Hypoplasia of pons	–

Note.—R = right; L = left; Ant = anterior; Sup = superior; CSA = chemical shift artifact; CC = corpus callosum; SP = septum pellucidum; CSP = cavum septum pellucidum; CV = cavum vergae; CPA = cerebellopontine angle; IAC = internal auditory canal.

^a Case 6, 0.3 T; cases 2–4, 0.35 T; cases 1 and 5, 0.5 T.

^b Biopsy proved.

^c Fat saturation images obtained as well.

^d No vessels; cranial nerve VII or VIII seen within lesion.

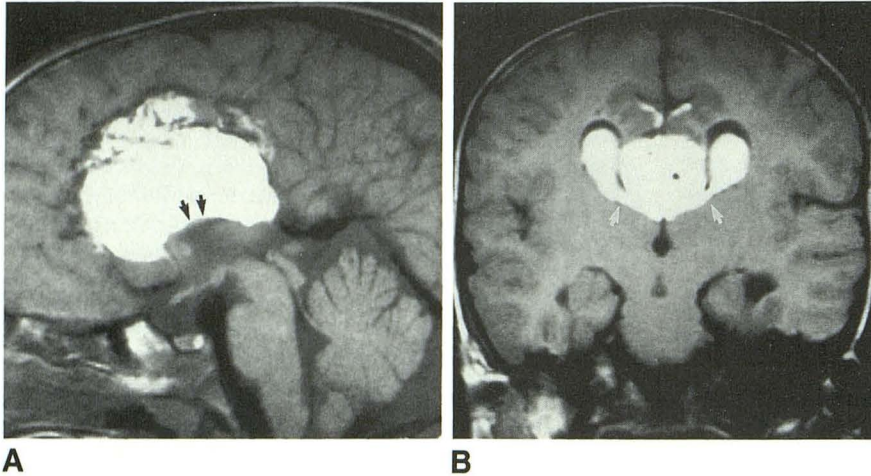


Fig. 1.—Case 7.
A and B, Midline sagittal (A) and coronal (B) T1-weighted images, 800/20/2, at 1.5 T reveal severe callosal hypoplasia (black arrows) and bulky, anterior lipoma with contiguous choroidal extension (white arrows). Note flow void in anterior cerebral artery.

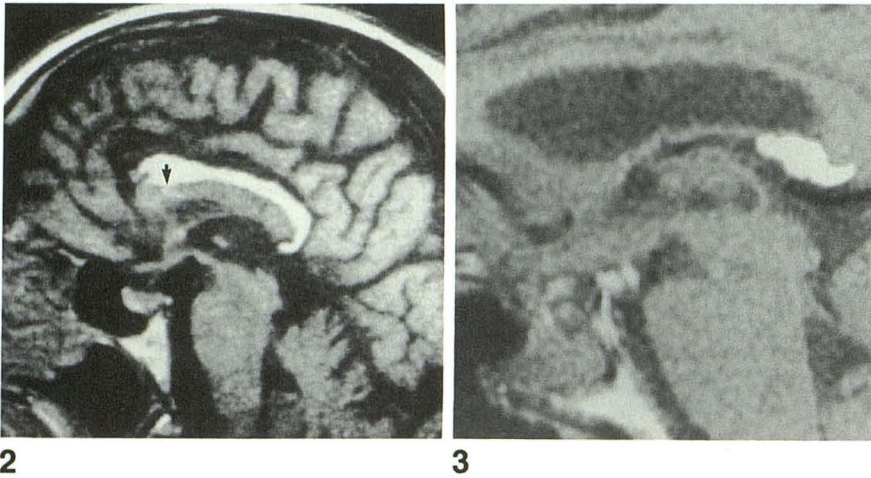


Fig. 2.—Case 3. Sagittal T1-weighted image, 500/40/1, at 0.35 T shows ribbonlike pericallosal lipoma and mild hypoplasia of dorsum of callosal body (arrow).

Fig. 3.—Case 21. Sagittal T1-weighted image, 800/15/1, at 1.5 T reveals lipoma of cistern of velum interpositum with retrosplenial tail.

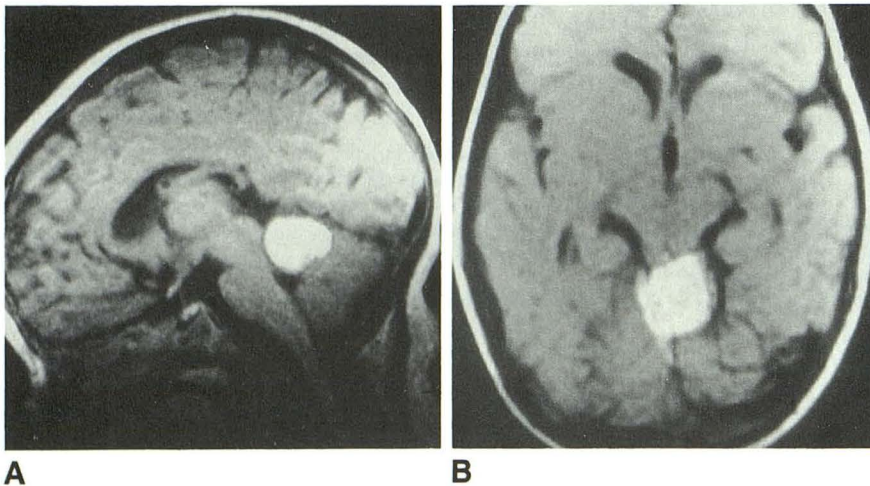


Fig. 4.—Case 6.
A and B, Sagittal T1-weighted image, 477/30/4 (A), and axial proton-density image, 2300/30/2 (B), at 0.3 T reveal hypoplasia of both left inferior colliculus and superior vermis.

Scattered accounts appeared until 1856, when Rokitansky first reported a lipoma of the corpus callosum [3]. Over the ensuing 63 years, numerous case reports and reviews on the subject of intracranial lipomas appeared [3–5, 9–18]. These reports have generated numerous theories on the pathogen-

esis of the intracranial lipoma; most of these hypotheses appear to be untenable. In 1863, Virchow proposed hypertrophy of preexisting fatty tissues of the meninges, the existence of which had already been described by Chiari, and subsequently by others [2]. In 1887, Taubner proposed that lipomas

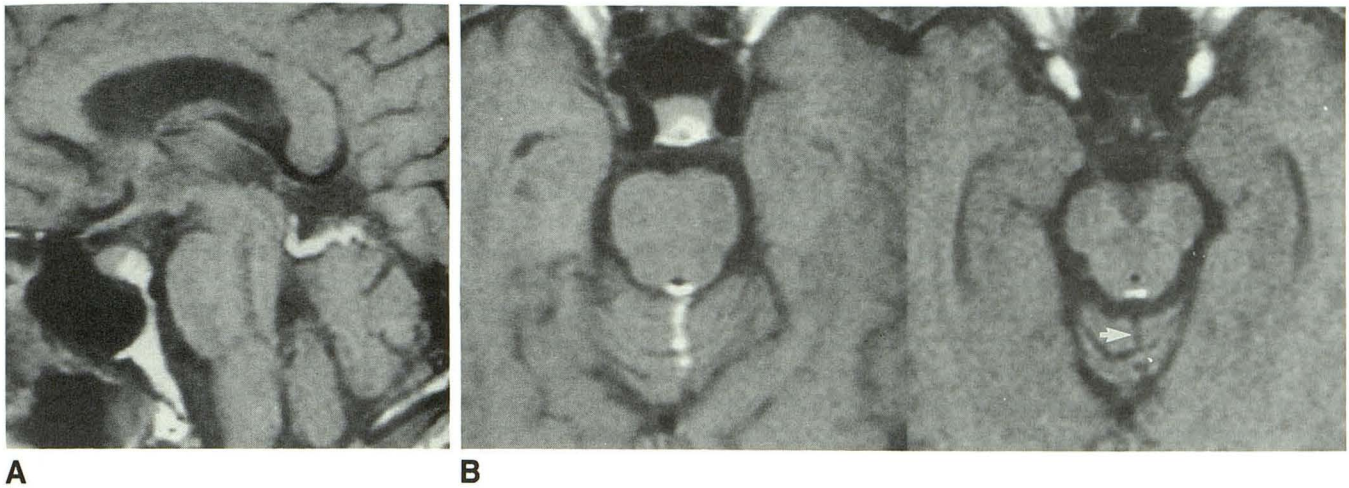


Fig. 5.—Case 25.
A and B, Sagittal (A) and axial (B) T1-weighted images, 600/20/2, at 1.5 T show lipoma between inferior colliculi and draped over vermis. Note mild superior vermian hypoplasia (arrow).

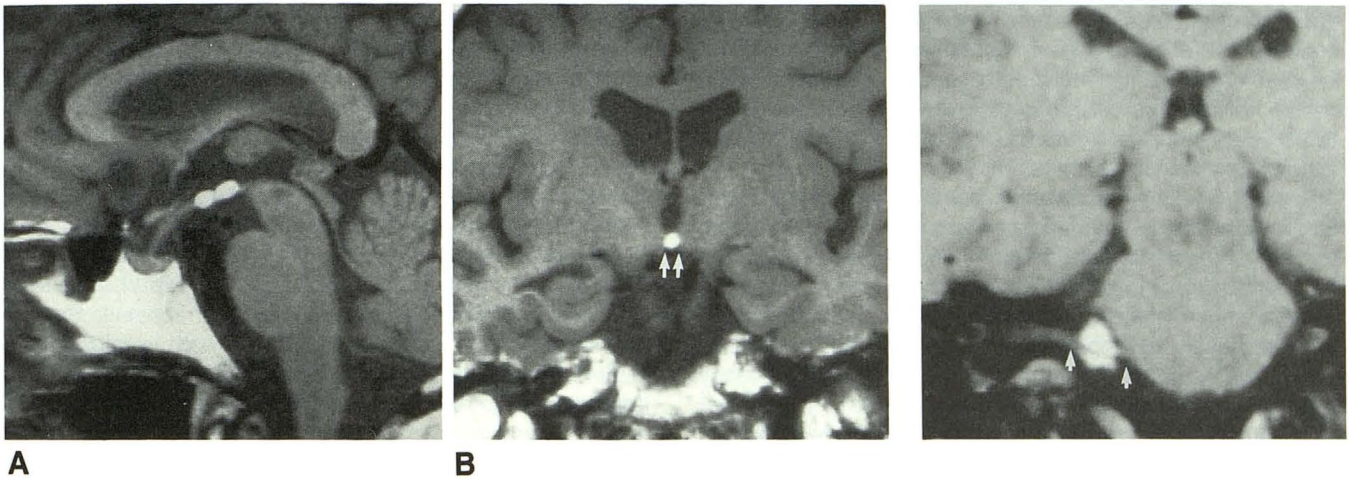


Fig. 6.—Case 32.
A and B, Sagittal (A) and coronal (B) T1-weighted images, 500/24/4, at 1.5 T reveal bilobed hypothalamic/mamillary body, suprasellar lipoma. Mamillary bodies are hypoplastic (arrows).

Fig. 7.—Case 38. Coronal T1-weighted image, 600/20/4, at 1.5 T shows seventh/eighth cranial nerve complex coursing through surgically proved right cerebellopontine angle lipoma (arrows).

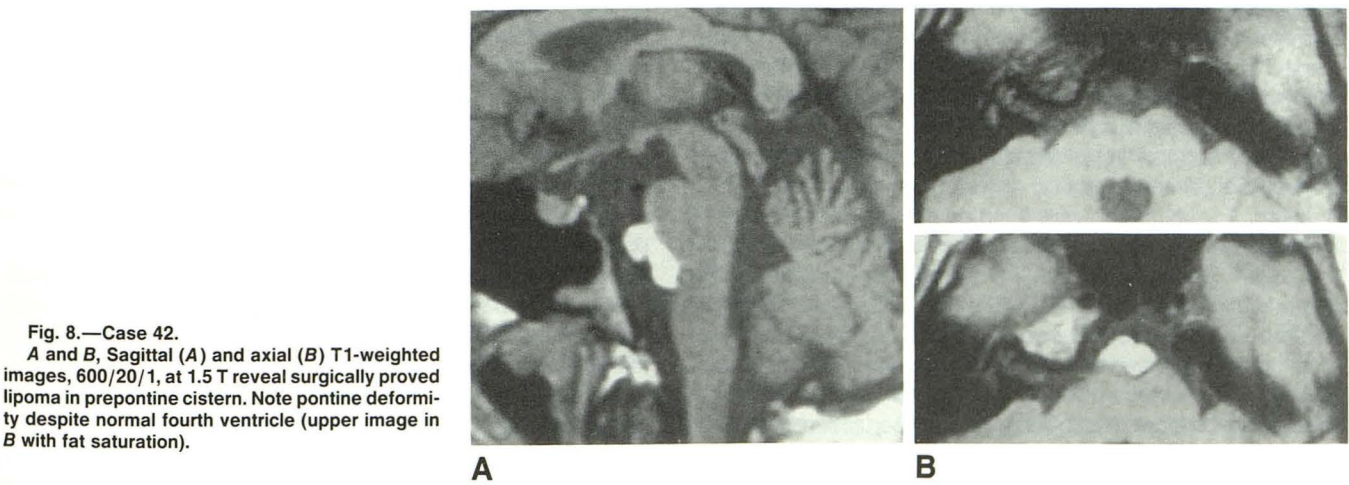


Fig. 8.—Case 42.
A and B, Sagittal (A) and axial (B) T1-weighted images, 600/20/1, at 1.5 T reveal surgically proved lipoma in pre-pontine cistern. Note pontine deformity despite normal fourth ventricle (upper image in B with fat saturation).

took their origin from within the brain substance, in the form of a lipomatous glioma [3, 10]. A third idea was suggested by Pugliese, who postulated that a transformation or metaplasia of meningeal connective tissue resulted in a lipoma [2].

These three theories, however, do not adequately explain several features of the intracranial lipoma. For instance, how could simple hypertrophy account for the associated congenital brain anomalies so frequently seen in cases of intracranial lipoma? The meninges are not yet clearly elaborated at the time of major structural organization of the brain. Thus, were hypertrophy to be the operative mechanism, any relation to congenital brain anomalies would be purely coincidental, as the gross structure of brain would otherwise be properly formed by the time the meninges "hypertrophied." Moreover, were hypertrophy to be the path of development, or were the lipoma to develop according to ideas of Taubner or Pugliese, would not the adjacent intracranial vessels, cranial nerves, and brain structures be displaced by, rather than incorporated within, the lipoma? As our results and those of most other authors show, such displacement is not the rule. Rather, the anterior cerebral vessels in the case of callosal lipomas, the middle cerebral branches in the case of sylvian lipomas, the trochlear nerve in the case of dorsal midbrain lipomas, and the seventh/eighth cranial nerve complex in the case of CPA cistern lipomas course through the lesions. In addition, the corpus callosum is not deformed secondary to mass effect; rather, it is hypogenetic.

In 1897, Bostroem suggested that the lipoma be grouped with intracranial dermoid and epidermoid tumors [2, 3]. Accordingly, he envisioned the lipoma as a displaced portion of the dermal anlage that differentiated into a lipoma while its other mesodermal elements receded. Bostroem's theory lost favor, however, as it too failed to account for the intralésional cerebral vessels and cranial nerves, as well as the frequency of dorsal cisternal involvement of lipomas. A fifth theory of origin suggests fatty degeneration of proliferated glia. As Zettner and Netsky [3] point out, however, lipomas of the CNS, like those of other parts of the body, consist of mature univacuolar adipose cells, not a disordered mass of catabolic debris.

The subsequent theory, of a mesodermal inclusion within the lips of the closing neural tube, finally addressed the question of associated congenital brain anomalies [2]. This idea holds that intracranial lipomas are part of a greater dysraphic state. Proponents of this concept tender the often-associated callosal hypoplasia and the rarely associated frontal bone defect with subcutaneous lipomatous extension as evidentiary support [11]. Unfortunately, this concept of disordered neurulation actually raises more questions than it answers. For instance, were such an inclusion to occur, the lesion would be expected to be primarily, if not wholly, intraventricular, hence facing the "inside" of the neural tube, the future ventricles and central canal of the spinal cord. Second, such an inclusion would be expected to exhibit mass effect on the intracranial vessels and nerves. It is unlikely that such vessels and nerves would ever be found within the lesion. Third, while the concept of disordered neurulation does address the frequent association of callosal hypogenesis, the cisternal lipomas and, in particular, the nonmidline lesions are

not adequately explained by this notion. Finally, and most significantly, the proposed validation of this pathogenetic theory is the demonstration of lipomatous tracts to the subcutaneous tissues [11]. This finding, purportedly conferring proof that lipomas arise from without and must be entrapped within the neural tube, is actually the weakest evidence of all. Were such a mechanism operative, subcutaneous lipomatous extension would be the rule and not the exception. Such reasoning is simply at odds with the findings in almost all cases. The only possible exception is in the rare case of the sphenoid encephalocele, in which case abnormal disjunction at the anterior neuropore could be related to the development of an intracranial lipoma. Thus, in the vast majority of cases, not only are intracranial lipomas not mesodermal inclusions, they cannot be.

The final theory of origin was first suggested by Verga [4] in 1929. Embracing Salvi's concept of the *meninx primitiva*, Verga suggested a development disorder relating to the *meninx*, although he regarded the lesion as a tumor. Shortly thereafter, Krainer [5] elaborated on the concept of Verga. In his critical review of intracranial lipomas, Krainer noted the cisternal nature of lipomas and stressed their nonneoplastic behavior, respecting and incorporating, rather than displacing, the intracranial vessels and nerves. Moreover, Krainer was the first to see the predilection for certain intracranial lipomas to occur in cisterns, although he did not explain this finding.

Discarding the prior pathogenetic theories, Krainer concluded that the concept of Verga was the most plausible. He suggested that an abnormal, persistent focus of *meninx primitiva* was somehow induced to differentiate into adipose and mature into a lipoma. This simple concept explains the subarachnoid, cisternal nature of intracranial lipomas; the absence of other mesodermal derivatives, such as muscle and cartilage; and the intralésional location of vessels and nerves. If lipomas were truly maldifferentiated *meninx*, the vessels and nerves would be expected to course through, not around, the lipoma. Such is the case, whether the lesion be pericallosal, sylvian, quadrigeminal/superior cerebellar, or CPA in location. Thus, the lipoma *is* maldifferentiated subarachnoid "space," and whatever courses through the cistern can course through the lipoma.

Ehni and Adson [9] and List et al. [10] further elaborated on this theory. In reviewing Wassermann's work on the fat-forming potential of neural crest, they noted that the *meninx primitiva* contains "primitive perivascular reticuloendothelium which, instead of subserving hematopoietic function, becomes specialized in the storage of fat" [10]. This finding of lipomatous differentiation of *meninx* explains why disturbances in the resorption of *meninx* result in lipomas and verifies that it is not necessary to invoke mesodermal elements in the development of these lesions.

Zettner and Netsky [3] addressed the matter of calcification and bone formation, common findings in intracranial lipomas. They stated that "the bony elements are foci of osseous metaplasia following calcification, a process frequently encountered elsewhere in the body." As noted by Bailey and Bucy [19], bone formation within lipomas is membranous, not enchondral, and mesodermally derived bone and cartilage have not been reported. Hence, another feature of intracranial

lipomas had been explained. However, yet unanswered were the questions of the associated brain anomalies and preferential sites. Regarding associated anomalies, Zettner and Netsky suggested a genetic etiology and considered the pericallosal lipoma and callosal hypogenesis as independent lesions. They did not address the predilection for certain cisternal locations, as their article focused only on pericallosal lipomas.

The answer to these latter questions relates to the formation of the subarachnoid cisterns, which was studied in great detail by Weed [20] in 1917. In his classic paper on the development of the cerebrospinal spaces, Weed cannulated both the lateral ventricle and central spinal canal of the pig embryo and replaced the CSF with potassium ferrocyanide and iron-ammonium citrate. He interpreted his findings as confirmation that the CSF is initially formed by the fourth ventricular choroid plexus. According to his experiments, CSF escapes the fourth ventricle via its thin dorsal wall and dissects through the extracellular space of the meninx primitiva. He postulated that the meninx resorbed as the CSF accumulated, leaving the subarachnoid cisterns. As a result of his studies, in which dye initially collected dorsal to the fourth ventricle and then spread ventrally around the brainstem, he reasoned that the subarachnoid space forms in that same sequence.

For over 70 years, the conclusions of Weed have been accepted. Unfortunately, scrutiny of his methodology reveals a critical flaw: he presumed that all CSF was elaborated by the choroid plexus (an accepted fact at that time), and that only after rupture of the dorsal fourth ventricle could CSF escape to form the cisterns. This presumption is evident by his selection of catheter placement; he replaced only the intraventricular contents and noted the dye's pattern of egress. However, if the cisterns had already started to form in areas other than the dorsal perirhombencephalic cisterns, his experiment would have yielded the same results. In fact, this appears to be the case.

As several authors have pointed out, the fourth ventricular choroid plexus does not form embryologically until Carnegie stage 19 (approximately 48 days), while cavitation of the meninx has already started at least by stage 18 (44 days), and possibly as early as stage 14 (32 days) [6, 21]. In addition, Osaka et al. [21] have shown that the cisterns develop in an orderly fashion quite different from that described by Weed. As seen in Figure 9A, the earliest primitive subarachnoid space appears ventral to the brainstem. With its progressive expansion, the future preontomedullary cisterns and anterior spinal subarachnoid space are created. Dorsolateral extension results in perimesencephalic and dorsal mesencephalic cisterns at stage 18 (41 days).

Thus, before the fourth ventricular choroid plexus is elaborated, much of the subarachnoid space has already started to form. At stage 18, the meninx remains in the areas dorsal to the future tectum, dorsal to the spinal cord, and anterior (both ventral and dorsal) to the telencephalon (Fig. 9B). By stage 20, much of the meninx has resorbed, leaving concentrations dorsal to the spinal cord, and lamina terminalis. By stage 23, only the last compact collection of meninx remains, located rostral (dorsal) to the lamina terminalis (Fig. 9C).

With the demonstration by Osaka et al. of orderly formation of the cisterns in mind, it is now possible to explain the various preferential cisternal sites of intracranial lipomas. As the region dorsal to the lamina terminalis is the last to clear, the window of opportunity for maldifferentiation of meninx is the greatest in this area. Hence, this is the most common site for intracranial lipomas to occur. Moreover, meninx is found within the banks of the lamina reuniens, the thickened dorsal portion of the primitive lamina terminalis that serves as a bed for ingrowth of the fibers of the corpus callosum (Fig. 10A) [22]. Persistence of such meninx could thus interfere with the proper closure of the sulcus medianus telencephali medii (SMTM) to form the massa commissuralis; furthermore, the degree of the resulting callosal hypoplasia would be related to the timing of the maldifferentiation of the meninx. An early problem, preventing formation of any massa commissuralis, would result in callosal agenesis. Maldifferentiation of the persistent meninx would result in either a lipoma of the cistern of the lamina terminalis or a bulky anterior interhemispheric lipoma, depending on the degree of meninx affected. A problem occurring slightly later would permit the development of a rudimentary, hypogenetic corpus callosum and a bulky, anteriorly situated, pericallosal lipoma (Fig. 10B). Larger lipomas presumably are related to greater degrees of hypogenesis because a greater amount of interhemispheric meninx remains present adjacent to the SMTM at the time of maldifferentiation as compared with the more dorsal lipomas, which tend to be smaller and associated with lesser degrees of hypoplasia. In fact, in our series, the smaller ribbonlike, dorsal lipomas were associated with either a dorsal groove in the callosal body or a hypogenetic posterior body and/or splenium (Fig. 10C). Similarly, extension via the choroidal fissures into the lateral ventricular choroidal plexuses would be expected in a significant percentage of pericallosal lipomas, particularly the larger, anterior ones that result from greater quantities of meninx [8]. In contradistinction to the reported frequency of choroidal extension (20%), we observed such extension in 73% of large anterior lipomas, 40% of smaller dorsal lipomas, and 62% overall. Finally, insults at stage 23 or 24, when nearly all the meninx has resorbed, minimally affect the corpus callosum, if at all, and result in a retrosplenial buttonlike lipoma, or a lesion within the cistern of the velum interpositum.

Other preferential sites of lipomas include the suprasellar and quadrigeminal/superior cerebellar cisterns. The pattern of dissolution of meninx described by Osaka et al. [21] would predict these locations, because the meninx remains concentrated ventral to the telencephalon and dorsal to the future quadrigeminal plate until late in the formation of the subarachnoid cisterns. Hence, it is not surprising to find lipomas in these cisterns.

Regarding suprasellar lipomas, it is interesting to note that all reported cases lie rostral to the expected location of Lillequist's membrane. In fact, of the 36 suprasellar lipomas reviewed by Verga [4], Krainer [5], Discepoli [23], and Wachter et al. [24], only one was reportedly situated within the interpeduncular cistern. That lesion, originally reported by deSteiger, was adjacent to the posterior perforated substance, rostral to Lillequist's membrane [5]. Our findings agree with this: five lipomas were suprasellar; one was inter-

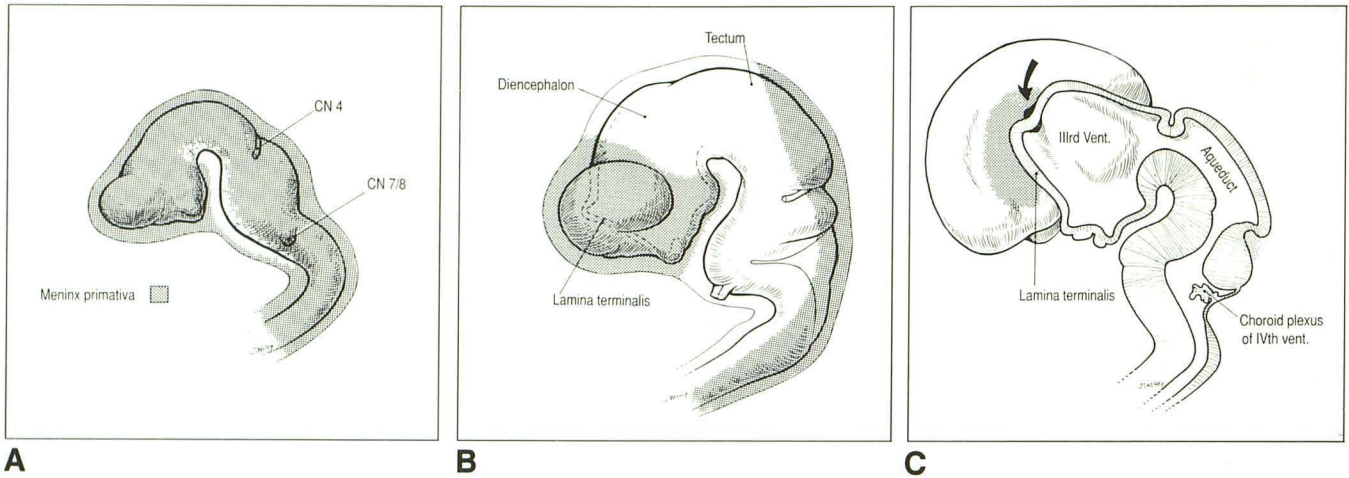


Fig. 9.—A, Left lateral view of embryo at approximately Carnegie stage 14 (32 days, 5–7 mm) reveals earliest cavitation of meninx primitiva ventral to brainstem. CN = cranial nerve.
 B, At stage 18 (44 days, 13–17 mm), further dissolution of meninx has occurred; residual meninx is seen rostral to leptomeningeal septum, around (and between) telencephalic vesicles and dorsal to mes- and rhombencephali.
 C, In composite midsagittal section over stages 19–23 (48–57 days, 17–30 mm), meninx is still present rostral (dorsal) to lamina terminalis and probably within future quadrigeminal/superior cerebellar cistern. Note close proximity of choroidal fissure (arrow) to interhemispheric meninx, accounting for extension of lipomas into lateral ventricular choroid plexuses. Vent. = ventricle.

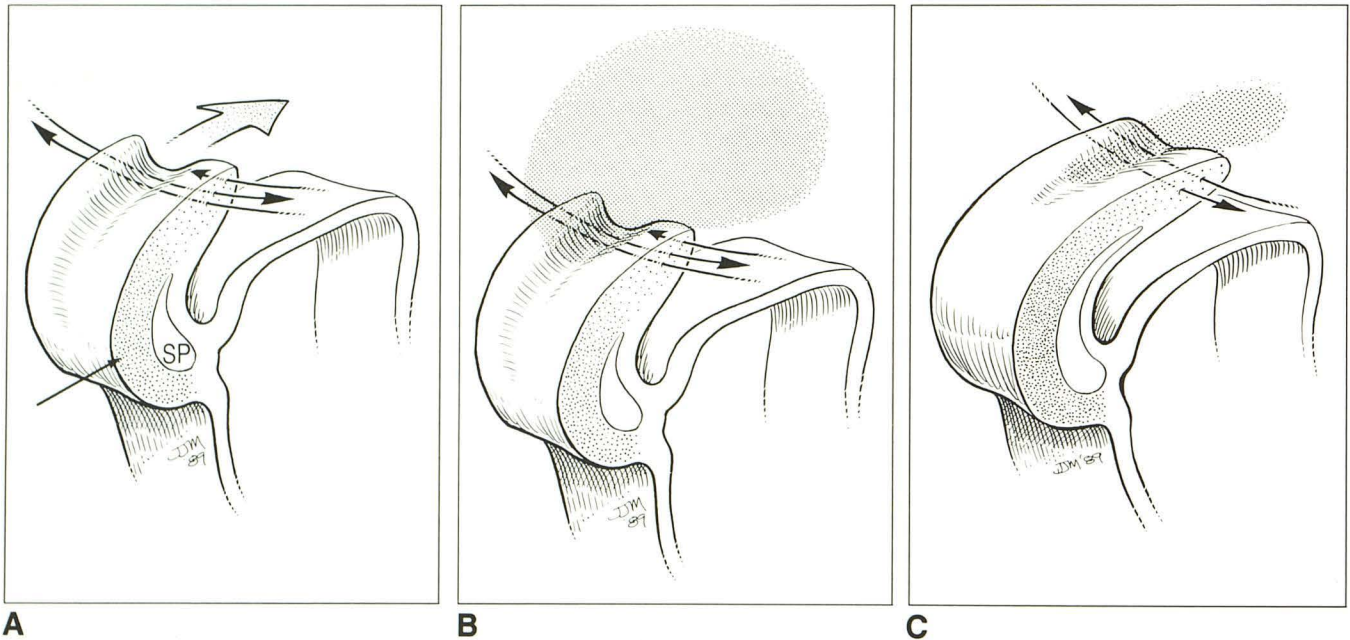


Fig. 10.—A, Conceptual view of early corpus callosum shows thick commissural plate anteriorly where hemispheric transcalsal fibers have already traversed (straight arrow). More posteriorly, dorsal callosal groove (sulcus medianus telencephali medii [SMTM] of text) is deeper where ingrowth of fibers is still in early stage (curved arrows). As growth occurs, callosum thickens, meninx (not shown) dissolves, and groove fills in. SP = septum pellucidum.
 B, Interhemispheric meninx is contiguous with that of dorsal callosal groove. An insult at this early stage results in severe callosal hypoplasia; if meninx persists, a “pericallosal” lipoma may develop.
 C, At a later stage of callosal development, much of interhemispheric meninx has cavitated, leaving that of dorsal callosal groove. An insult at this stage would interfere with proper thickening of callosal body and splenium and result in dorsal ribbon lipoma or retrosplenial button.

peduncular, yet dorsal to the expected location of Lillequist’s membrane. Moreover, that lipoma was associated with a second lipoma of the mamillary body. Thus, to date, no lipoma has been reported within the interpeduncular cistern, deep to Lillequist’s membrane, or in the prepontine cistern.

The fact that lipomas do not occur caudal to Lillequist’s membrane can be explained by its embryologic derivation. At approximately Carnegie stage 16 or 17, a condensation of meninx primitiva forms a leptomeningeal septum that will become the medial extent of the future tentorium [6]. The

remainder of the tentorium is derived from pachymeningeal tissues. With maturation, the leptomeningeal medial portion regresses at approximately Carnegie stage 23 and later. Its vestige appears to be the thin arachnoid veil known as Lillequist's membrane, which separates the subarachnoid spaces of the telencephalon and diencephalon from those of the mesencephalon and rhombencephalon. Cavitation of the meninx primitiva secondary to expansion of the intercellular space can proceed rostrally from the prerhombencephalic areas only as far as the leptomeningeal septum, since this process occurs before the regression noted in stage 23. The intercellular expansion is forced dorsolaterally, and only after bypassing the septum can the basal telencephalic and diencephalic cisterns develop. Hence, the meninx primitiva persists longer in the suprasellar region and permits the errant lipoma to occur. Prior to this report, no lipomas have been reported deep (caudal) to the leptomeningeal septum, where the meninx cavitates early. Nevertheless, because meninx primitiva briefly fills the prerhombencephalic region, the potential exists for a lipoma to develop. The present series includes one such case (Fig. 8), which must represent a very unusual occurrence.

In his review of lipomas of the tuber cinereum, Discepoli [23] noted distortion of the neural architecture and was unable to identify a clear boundary between the lipoma and the tuber cinereum in his two cases. Wachter et al. [24] noted deficient pia between the extraaxial lipomas and hypogenetic mamillary bodies. Thus, suprasellar lipomas are in accordance with the findings of Osaka et al. [21] regarding the dissolution of the meninx. As they are not inclusions, but malformations of the subarachnoid spaces, lipomas would be expected to be associated with hypogeneses of adjacent neural structures that would develop improperly because of the lack of regression of meninx primitiva.

Similar findings relate to lipomas of the quadrigeminal/superior cerebellar cisterns. Maiuri et al. [25], in a review of 26 previously reported cases and one of their own, noted a consistent relationship of dorsal mesencephalic lipomas to the inferior colliculus and, to a variable degree, the superior medullary velum, superior cerebellar peduncles, and superior vermis. The trochlear nerve usually passes through the lipoma as it does through the normal cistern. In our series, radiographically detectable abnormalities of the adjacent neural structures were demonstrated in five of 11 lesions of the quadrigeminal/superior cerebellar cisterns, although we were unable to reliably detect the trochlear nerves either within or outside the lipomas.

Finally, two additional sites merit attention. Less common than those already addressed are lipomas of the CPA and sylvian cisterns; both locations are consistent with the findings of Osaka et al. [21]. CPA lesions typically relate to the pontomedullary sulcus, wherein the meninx may be trapped despite its dissolution in the ventral rhombencephalic cisterns. Moreover, as the seventh and eighth cranial nerve complex passes through the cistern, one or both nerves may course through the lipoma and carry the lipoma to the IAC.

Leibrock et al. [26] reviewed the 11 reported cases of CPA lipomas. They suggested that "lipomas usually occur at junctions between the segments of the central nervous system,"

including the pontomedullary junction. As these junctions represent sites of neural tube flexion, they are sites of redundant meninx primitiva. Hence, they possess greater opportunity for the development of lipomas. These authors also noted incorporation of the eighth nerve within the lipoma in all cases. In our series, the images revealed such incorporation in two of the four CPA/IAC lipomas.

Very few cases of sylvian lipomas have been reported. Dyck [27] noted branches of the middle cerebral artery (MCA) traversing the lipoma in a patient with auditory hallucinations. One of our cases demonstrated flow void within the lipoma representing MCA branches. While Dyck offered no information regarding pathogenesis, both the findings of Osaka et al. [21] and the suggestion of Leibrock et al. [26] of arachnoid (meninx) redundancy would appear to apply.

Thus, by merging the initial concept of Verga of persistence and maldifferentiation of meninx primitiva with the data of Osaka et al. regarding the orderly dissolution of meninx and creation of the subarachnoid cisterns, a unified developmental concept is apparent. There remains, however, one final developmental question: how can the rare lipomatous extension into the subcutaneous tissues be explained? Rather than an abnormality of inclusion, we concur with Kudoh et al. [28] and believe the opposite is more likely. In patients with midline facial dysraphism, there is likely secondary dehiscence of the future anterior cranium with the potential evagination of a small finger of meninx primitiva. In this way, the intracranial lipoma could be contiguous with a subcutaneous lipoma, or could be isolated if the vault subsequently excluded the two embryologically related segments.

In general, intracranial lipomas are asymptomatic and require no therapy. As noted above, both vessels and nerves typically course through the lipomas, making the surgical approach technically difficult and hazardous [12]. There are, however, two exceptions in which surgery does have a role. The first relates to the obvious cosmetic deformity consequent to the rare frontal lipoma. While removal of the extracranial component is feasible, extirpation of the intracranial lesion, contiguous or separate, should not be attempted. Nearly all cases of surgical removal of interhemispheric lipoma have yielded fatal results.

The second situation refers to the rare association of hydrocephalus with a quadrigeminal cistern lipoma. Including our patient, seven such cases have been reported [25]. It remains unclear, however, what relationship, if any, exists between the lipoma and hydrocephalus. One possibility is compression of the inferior aqueduct secondary to somatic growth of the lipoma. Alternatively, the hydrocephalus may be due to inflammation with consequent adhesions resulting from a viral or chemical meningitis. A last possibility is that the aqueductal stenosis is congenital and unrelated. If unrelated, however, we would not expect to see hydrocephalus exclusively in association with quadrigeminal lipomas, but in association with other intracranial lipomas as well.

In conclusion, intracranial lipomas tend to occur in specific, characteristic locations within the brain. Furthermore, at least half of these lipomas are associated with other brain anomalies. We believe that these lesions are themselves congenital malformations that result from abnormal persistence and

maldifferentiation of meninx primitiva during the development of the subarachnoid cisterns. The proposed theory, as explained in this article, seems to explain all of the observed characteristics of these anomalies.

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The reader's attention is directed to the commentary on this article, which appears on the following page.