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A Cliniconeuroradiologic Approach to Third Cranial Nerve Palsies

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Sixty-three patients with third cranial nerve palsies (CNPs), either isolated (31) or in association with other neurologic deficits (32), underwent neuroophthalmologic and neuroradiologic evaluation. Discrepancies between the clinical and radiologic evaluations were analyzed and useful clinical presenting symptoms were identified. Microvascular infarction secondary to diabetes mellitus and/or hypertension was the most common cause in patients with isolated third CNP, and extensive neuroradiologic evaluation is not indicated in this subgroup. The overall diagnostic yield of high-resolution CT for isolated third CNPs was low (30%), but improved to 60% if diabetes and hypertension were excluded. However, CT was highly sensitive (90%) in those patients with third CNPs associated with additional neurologic deficits. The status of the pupil in and of itself cannot be the sole determinant as to whether angiography is indicated to exclude an aneurysm. Careful ophthalmologic observation and relating the severity of pupillomotor dysfunction to extraocular ophthalmoplegia is mandatory to determine the logical sequence of radiologic evaluation. Retroorbital pain taken in isolation is a nonspecific presenting symptom and has differential diagnostic value only if it is correlated temporally with the onset of third CNP and the presence or absence of additional cranial nerve deficits.

Distinguishing patients with third cranial nerve palsy (CNP) secondary to ischemic microvascular disease from those with structural lesions in the brainstem, circle of Willis, cavernous sinus, and orbital apex is a common clinical problem. In patients with ischemic third CNP extensive radiologic evaluation is not indicated in view of the high prevalence of diabetes mellitus, the most common cause of such lesions. The palsies can be broadly divided into those with external (extraocular ophthalmoplegia) and those with internal (pupillary) dysfunction; the degree of involvement in each can vary from partial to complete. While the majority of isolated third CNPs with pupil sparing are due to diabetes and those with pupil involvement are due to expanding posterior communicating artery aneurysms, atypical cases from either cause can overlap and mimic each other. Fortunately careful clinical neuroophthalmologic examination can, in most cases, distinguish between ischemic and structural third CNPs.

The roles of CT in the evaluation of cavernous sinus/orbital lesions [1–4] and carotid angiography in the evaluation of posterior communicating artery (PCA) aneurysm are well established [5]. However, we are unaware of any report devoted exclusively to studying the efficacy of current neuroradiologic techniques in the evaluation of patients with third CNP and comparing these studies with the efficacy of clinical evaluation. In this article the discrepancies between the clinical and radiologic evaluations of 63 patients with third CNPs are analyzed and an algorithm based on this analysis is presented.

Anatomy

The nucleus of the oculomotor nerve consists of an elongated mass of cells lying

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in the inferior periaqueductal gray matter of the mesencephalon. In addition to motor neurons, the oculomotor nucleus contains cells whose axon projects as preganglionic, parasympathetic fibers to the ciliary ganglion for control of pupillary constriction and accommodation. From the ventral aspect of the oculomotor nucleus, axonal fibers traverse between the red nucleus and substantia nigra to exit the brainstem through the interpeduncular fossa [6]. The cisternal segment of the oculomotor nerve then passes between the peduncular segment of the posterior cerebral artery and the superior cerebellar artery, inferolateral to the PCA and medial to the free edge of the tentorium (Fig. 1). Pupilloconstrictor fibers are located superficially along the dorsomedial portion of the nerve, accounting for its high frequency of involvement in the presence of an expanding PCA aneurysm. The vascular supply of the third nerve in the subarachnoid space and the cavernous sinus includes branches originating from the proximal segment of the posterior cerebral artery, dorsal meningeal and inferior hypophyseal branches of the meningohypophyseal trunk, and the recurrent branch of the ophthalmic artery.

Within the cavernous sinus, the third nerve is located superior to the trochlear, abducens, and the first two divisions of the trigeminal nerves. The third nerve divides into two trunks after entering the orbit via the superior orbital fissure. The superior trunk innervates the superior rectus and the levator palpebrae superioris. The inferior trunk innervates the medial rectus, inferior rectus, and inferior oblique muscles; it also transmits preganglionic parasympathetic fibers to the pupil by way of the ciliary ganglion. Sympathetic pupillary fibers from the superior cervical ganglion ascend with the internal carotid artery and joins the ophthalmic division of the fifth nerve to reach the iris.

Materials and Methods

From October 1981 to April 1986, 73 patients were evaluated by the neuroophthalmology department at New England Medical Center Hospitals for suspected third CNPs. Sixty-three of these patients underwent neuroradiologic evaluation (62 patients had CT, 30 had angiography, and four had MR). The clinical and neuroradiologic evaluation of the 63 patients is the subject of this report. After reviewing the clinical presentation with the referring neuroophthalmologist, we determined a tailored sequence of radiologic evaluation depending on whether the orbit, parasellar region, supratentorial region, or brainstem area was suspected of being involved. All patients were scanned with a modern CT scanner (Siemens Somatom II or DR3). Cerebral angiograms were all obtained selectively with magnification techniques. MR scans were obtained on a 1-T unit (Siemens Magnetom). Spin-echo (SE) sequences were performed with several different repetition (TR) and echo delay (TE) times. The final diagnosis was based on either clinical follow-up, response to appropriate therapy, surgery, or unequivocal radiologic findings.

Results

The 63 patients were subdivided into six categories on the basis of clinical presentations (Tables 1 and 2): *category 1*—complete external third CNP with pupil sparing (17 patients); *category 2*—complete external third CNP with partial pupil involvement/relative pupil sparing third CNP (two patients); *category 3*—partial external third CNP with partial pupil involvement (three patients); *category 4*—complete external and internal third CNP (11 patients); *category 5*—complete external third CNP (with or without pupil involvement) and additional cranial nerve dysfunction (16 patients); and *category 6*—complete external and internal third CNP with additional neurologic deficits (14 patients).

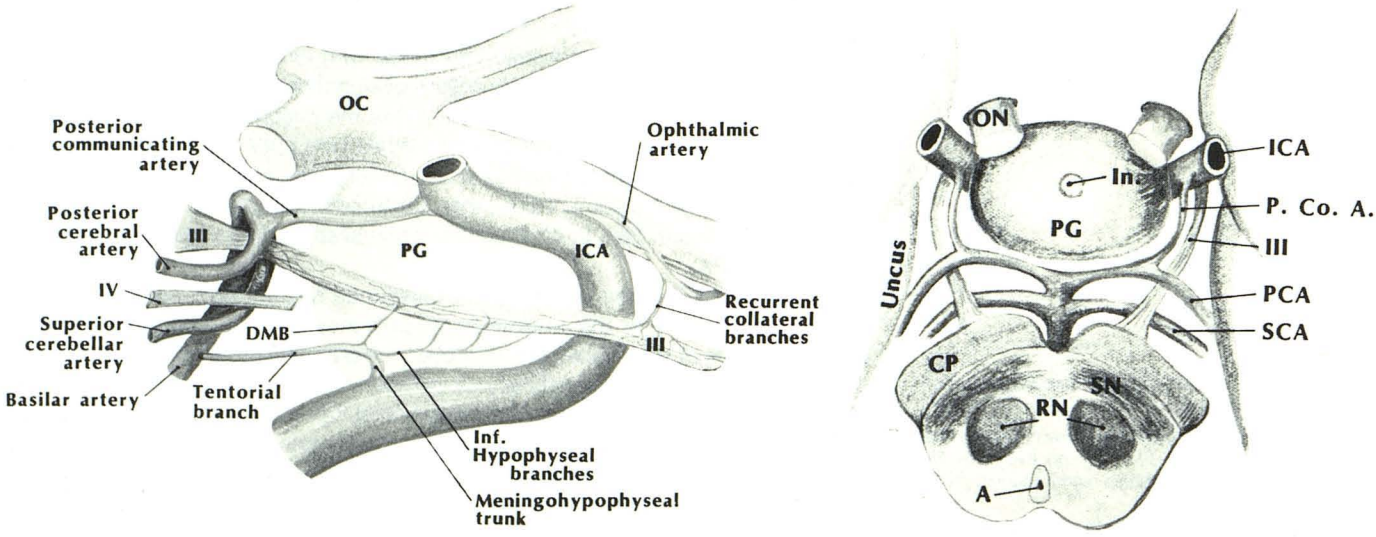


Fig. 1.—Vascular supply of cisternal segment of third (III) cranial nerve and its relationship to posterior communicating artery. OC = optic chiasm; PG = pituitary gland; ICA = cavernous internal carotid artery; DMB = dorsal meningeal branch of meningohypophyseal trunk; Inf. = inferior; ON = optic nerve; In. = infundibulum; P. Co. A. = posterior communicating artery; PCA = posterior cerebral artery; SCA = superior cerebellar artery; CP = cerebral peduncle; SN = substantia nigra; RN = red nucleus; A = aqueduct.

TABLE 1: Final Diagnoses in Patients with Third Cranial Nerve Palsies

Category: Final Diagnosis	No. of Patients
1. Complete external third CNP with pupil sparing:	
Ischemic third CNP	14
Ophthalmic migraine	1
Myasthenia gravis	1
Idiopathic third CNP	1
Subtotal	17
2. Complete external third CNP with partial pupil involvement:	
Ischemic third CNP	2
3. Partial external third CNP with partial pupil involvement:	
Meningeal carcinomatosis	1
Tentorial meningioma	1
Basilar artery aneurysm	1
Subtotal	3
4. Complete external and internal third CNP:	
PCA aneurysm	5
Basilar artery aneurysm	1
Epidermoid	1
Cavernous angioma	1
Pituitary adenoma	1
Postviral mononeuritis	1
Posttraumatic	1
Subtotal	11
5. Complete external third CNP, with or without pupil involvement, and additional cranial nerve dysfunction:	
Pituitary adenoma	3
Giant cavernous carotid aneurysm	3
Orbital pseudotumor	2
Sphenoid wing meningioma	2
Trigeminal schwannoma	1
Tolosa-Hunt syndrome*	1
Orbital apex metastasis	1
Sphenoid wing fracture	1
Mucocele	1
Meningeal carcinomatosis	1
Subtotal	16
6. Complete external and internal third CNP with additional neurologic deficits (midbrain):	
Cryptic arteriovenous malformation	2
Glioma	2
Basilar artery thrombosis	1
Primitive neuroectodermal tumor	1
Subtotal	6
Complete external and internal CNP with additional neurologic deficits (supratentorial):	
Hematoma	2
Extraaxial fluid collection	3
Glioma	1
Posttraumatic	2
Subtotal	8
Total	63

Note.—PCA = posterior communicating artery; CNP = cranial nerve palsy.

* Painful ophthalmoplegia with enlargement of right cavernous sinus that responded to steroid therapy.

Category 1

All 17 patients with complete external third CNP with pupil sparing had high-resolution, 2-mm, axial, contrast-enhanced CT through the circle of Willis and cavernous sinus. The scans were all negative except for two patients: a patient with myasthenia gravis and an incidental aneurysm at the peduncular segment of the posterior cerebral artery (Fig. 2) contralateral to the ptosis and retroorbital pain, and a patient with incidental bilateral orbital varices. Carotid and vertebral angiograms in four patients did not contribute additional diagnostic information. Angiography was performed in one patient with known diabetes because pupil-sparing third CNP progressed to complete pupillary dysfunction ipsilateral to the retroorbital headache on follow-up ophthalmologic examination. Ischemic third CNP secondary to diabetes (either alone or in conjunction with hypertension) was the final diagnosis in 14 of 17 patients. On follow-up, the third CNP improved spontaneously at 5–10 weeks in all patients except the one with idiopathic third CNP. There was no aberrant regeneration, a phenomenon due to misdirection of regenerating axonal fibers that often occurs after injury to the oculomotor nerve. The regenerated axon that previously innervated one extraocular muscle may ultimately innervate another muscle or the ciliary ganglion. Clinically this results in either pupillary constriction or gaze/eyelid synkinesis when the patient is asked to look in a direction requiring oculomotor nerve function. Retroorbital pain was the presenting symptom in 10 of 17 patients. Localization of the lesion responsible for third CNP based on history and physical examination was correct in all except the patients with myasthenia gravis and idiopathic third CNP.

Category 2

Complete external third CNP with partial pupil involvement was found in two patients, and high-resolution contrast-enhanced CT through the circle of Willis was normal in both. Persistence of relative pupil sparing and retroorbital pain in one patient led to bilateral carotid and vertebral angiography. Angiography was not performed in the other patient because the relative pupil-sparing third CNP converted to a pupil-sparing third CNP on follow-up. The initial clinical and final diagnoses were diabetic ischemic third CNP in both cases, and the third nerve dysfunctions improved spontaneously within 4 weeks.

Category 3

Partial external third CNP with partial pupil involvement was found in three patients. High-resolution contrast-enhanced CT showed a small tentorial meningioma in one patient and abnormally prominent basal cistern enhancement in another patient with known pineoblastoma (Fig. 3). A routine contrast-enhanced CT scan in the third patient showed a giant basilar tip aneurysm. The first two patients presented with unilateral superior and medial recti dysfunction, while an isolated inferior rectus palsy was noted in the third patient. Carotid and vertebral angiograms were nondiagnostic in the patient with the tentorial meningioma. Angiography in the third patient

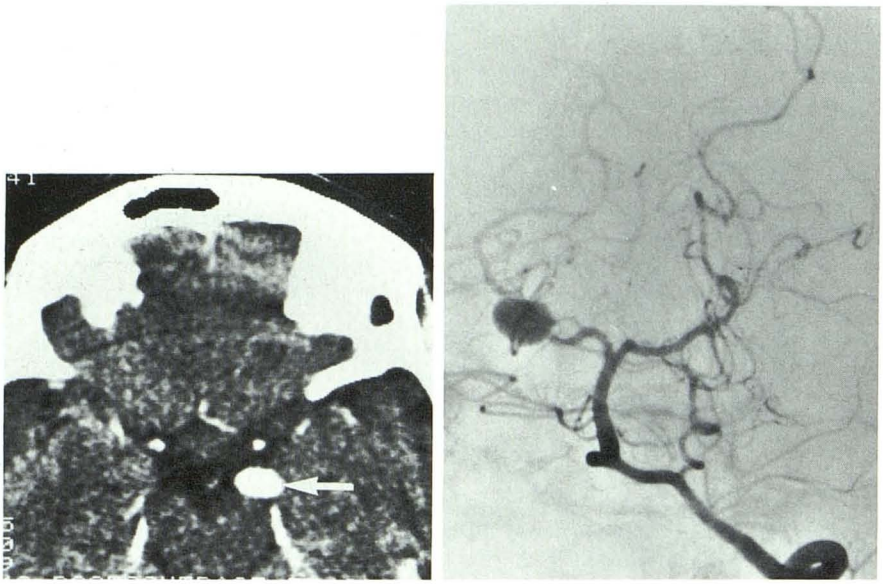
TABLE 2: Clinical and Radiologic Features of Third Cranial Nerve Palsies

Feature	Diagnostic Category					
	1 (n = 17)	2 (n = 2)	3 (n = 3)	4 (n = 11)	5 (n = 16)	6 (n = 14)
Retroorbital pain	10	2	1	8	11	0
Pupil sparing:						
Total	17	0	0	0	3	0
Relative	0	2	0	0	1	0
Partial	0	0	3	0	0	0
Pseudo	0	0	0	0	1	0
Additional cranial nerve deficits	0	0	0	0	16[a]	6[a]
Additional neurologic deficits	0	1[b]	1[b]	1[b]	0	14[b]
Lesion responsible for third CNP localized by CT	0	0	3	7/10	16	12
Cause of third CNP identified by angiography	0/4	0/1	1/2	6/8	5/6	3/9
Clinical localization correct	15	2	2	11	15	14

Note.—CNP = cranial nerve palsy.

[a] Additional cranial nerve deficits: category 5—cranial nerves II (10), IV (three), V_1 (four), V_2 (three), V_3 (one), V motor (one), VI (seven), VII (one); category 6—cranial nerves II (one), III (contralateral) (two), IV (one), VI (one), VII (three), X (one).

[b] Additional neurologic deficits: category 2—ataxia (one); category 3—ataxia, vertigo, and nystagmus (one); category 4—comatose (one); category 6—long tract signs (14).



A B

Fig. 2.—Incidental posterior cerebral artery aneurysm (*arrow*) at peduncular segment on contrast-enhanced CT scan (*A*) and anteroposterior view of left vertebral angiogram (*B*) in patient with myasthenia gravis.

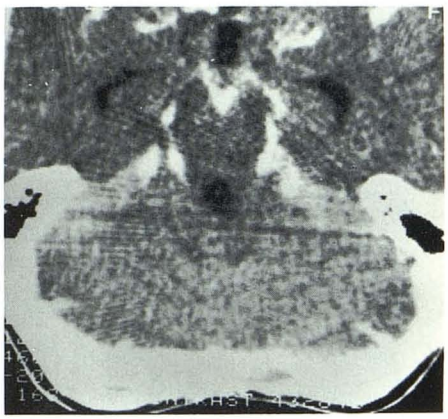


Fig. 3.—Abnormally prominent enhancement within peduncular and perimesencephalic cisterns in 17-year-old patient with known CSF seeding of pineoblastoma. Enlargement of temporal horns is from communicating hydrocephalus. Patient presented with weakness of right superior rectus and medial rectus, ptosis, and mildly dilated pupil.

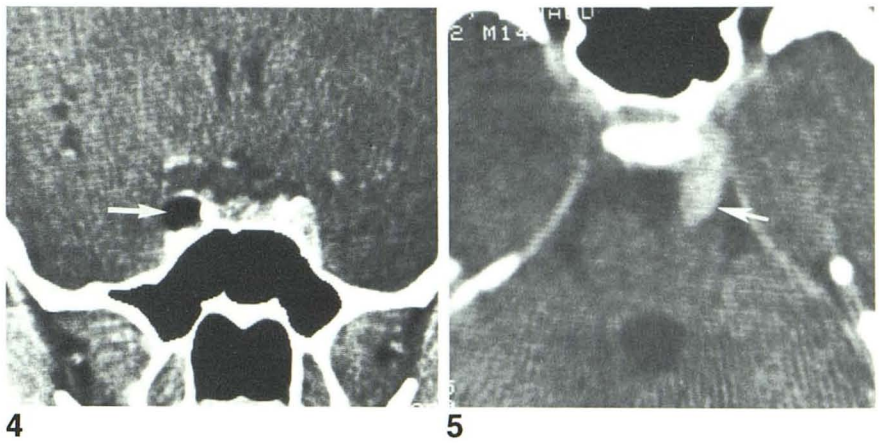
confirmed a giant basilar tip aneurysm and an incidental PCA aneurysm contralateral to the clinically apparent third CNP. Retroorbital pain was the presenting symptom only in the patient with the basilar artery tip aneurysm. There was no spontaneous improvement of the third CNP within this group. The patient with an angiographically proven giant basilar tip aneurysm was misdiagnosed clinically as brainstem glioma on the basis of history and physical examination.

Category 4

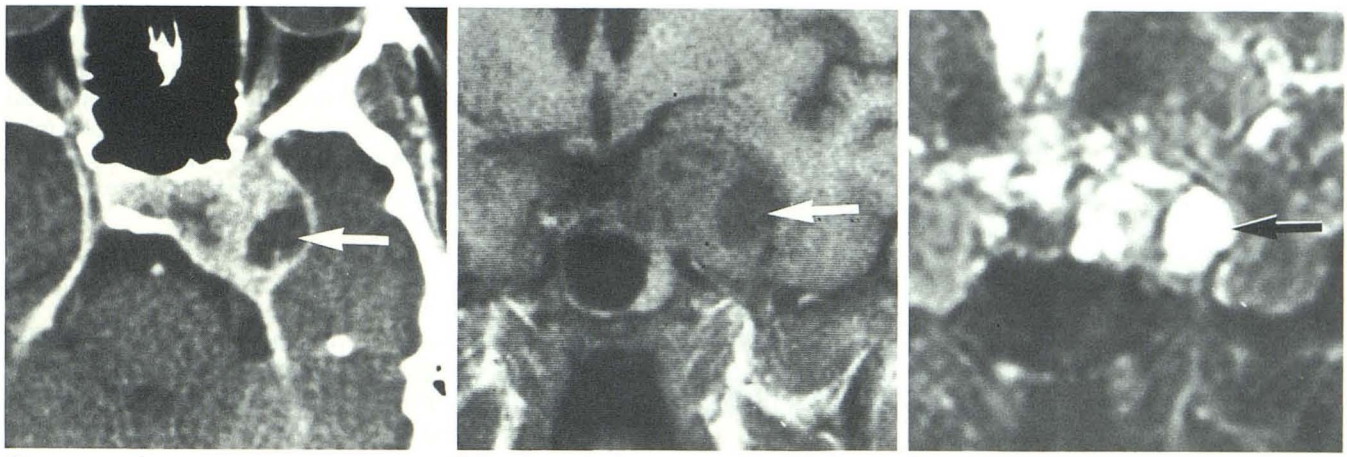
Complete external and internal third CNP was found in 11 patients. CT was performed in 10 of these. Unenhanced CT in four patients showed subarachnoid hemorrhage in two, while the scans were normal in one patient with bilateral PCA aneurysms and in another who had had head trauma many years before. High-resolution contrast-enhanced CT through

Fig. 4.—Direct coronal CT shows low-attenuation lesion (*arrow*) within right cavernous sinus in 24-year-old man with 3-week history of complete third nerve palsy and retroorbital throbbing headache. Working diagnosis of epidermoid tumor lacked surgical proof.

Fig. 5.—Fusiform enhancement along course of third nerve on left side (*arrow*) in 14-year-old boy who presented with complete third nerve palsy and retroorbital pain. Pathologic diagnosis was cavernous angioma of the third nerve.



4 5



A B C

Fig. 6.—49-year-old woman with 4-month history of diplopia and left-sided ptosis. Dysfunction of cranial nerves III, IV, VI, and V (all three divisions) was present on left side.

A, Contrast-enhanced CT shows marked lateral bulging of left cavernous sinus and eccentric area of low attenuation (*arrow*).

B, MR image. Coronal T1-weighted SE sequence (TR/TE = 0.6 sec/17 msec) shows area of hypointense signal in left cavernous sinus (*arrow*) corresponding to low density seen on CT.

C, Coronal T2-weighted SE sequence (TR/TE = 2.5 sec/140 msec) shows high-intensity signal (*arrow*). Surgery revealed partially necrotic trigeminal schwannoma.

the circle of Willis and cavernous sinus in the other six patients showed two PCA aneurysms, one cavernous sinus epidermoid tumor (Fig. 4), one cavernous angioma of the third nerve (Fig. 5), and one pituitary adenoma with cavernous sinus invasion. High-resolution contrast-enhanced CT was nondiagnostic in one patient with postviral mononeuritis. Eight patients had carotid and vertebral angiograms; six of these were diagnostic (five PCA aneurysms and one basilar artery aneurysm). Angiograms in the patients with postviral mononeuritis and third nerve cavernous angioma did not contribute additional diagnostic information. The decision to perform angiography was based on a combination of CT findings and pupillary dysfunction. Retroorbital pain was the presenting symptom in eight of 11 patients, while pupil sparing was not seen in any patients. Follow-up showed that a third CNP in the patient with postviral mononeuritis had resolved spontaneously within 5 weeks.

Category 5

Complete external third CNP (with or without pupil involvement) and additional cranial nerve dysfunction were found in 16 patients. High-resolution contrast-enhanced CT through the orbit and parasellar region in all 16 patients was successful in localizing the cause of the third nerve palsies. CT alone showed positive findings in 11 of the patients and provided a strong clue to the eventual diagnoses in five; these diagnoses were confirmed by either angiography (three giant cavernous carotid aneurysms) or biopsy (one orbital pseudotumor and one trigeminal schwannoma) (Fig. 6). Three additional patients underwent selective internal carotid angiography. A characteristic tumor blush was seen in the two sphenoid wing meningiomas, while circumferential encasement of the cavernous carotid artery was noted in the patient with trigeminal schwannoma. Retroorbital pain was a presenting symptom in

the three patients with giant cavernous carotid aneurysms; in two of the three patients with pituitary adenomas; in the patients with orbital pseudotumor, trigeminal schwannoma, Tolosa-Hunt syndrome, and orbital apex metastasis; and in a patient with meningeal carcinomatosis. True pupil sparing was noted in three patients (one pituitary adenoma with cavernous sinus invasion, one orbital pseudotumor, and one Tolosa-Hunt syndrome). Pseudosparing and relative sparing of the pupil were noted in one patient with giant cavernous internal carotid aneurysm and in one patient with sphenoid wing fracture, respectively. Concomitant CNPs involving the second (10 patients), fifth (seven patients), and sixth (seven patients) cranial nerves were the most common. Localization of the lesion responsible for third CNP based on history and physical examination was correct in all except the patient with the sphenoid wing fracture. Aberrant regeneration of the third nerve was encountered at follow-up in one patient with orbital pseudotumor.

Category 6

Complete external and internal third CNP with additional neurologic deficits was found in 14 patients. Lesions responsible for third CNPs were localized by CT to the midbrain in six cases. Selective vertebral angiography provided diagnostic information only in the patient with midbrain infarct secondary to basilar artery thrombosis. MR in a patient with an angiographic cryptic arteriovenous malformation (Fig. 7), a primitive neuroectodermal tumor (Fig. 8), and a midbrain glioma all provided additional diagnostic information. Hemiparesis or hemisensory loss, either isolated or in conjunction with other CNPs, was present in the six patients.

Supratentorially, routine CT showed the cause of third CNP in six of eight patients. CT was nondiagnostic in the two posttrauma patients. Carotid angiography in the two patients with parenchymal hematoma showed a giant anterior communicating artery aneurysm and a parietal arteriovenous malformation, respectively. While long-tract signs were present in all eight patients, six of the patients also had clinical and CT evidence of uncal herniation. Central seventh CNP and aberrant regeneration of the third cranial nerve were present in one posttrauma patient. Pupil sparing and retroorbital pain were not clinical features in any of the 14 patients. Localization of the lesion responsible for the third CNP based on history and physical examination was correct in all 14 cases.

Discussion

A third CNP may result from a lesion located anywhere along the course of the oculomotor nerve. The spectrum of diseases that can involve the third nerve is wide. The differential diagnosis depends on the age group and the clinical presentation [7–12]. The logical approach to the workup is to separate those patients with isolated third CNP from those with additional neurologic deficits (labeled here *complex third CNP*), since the relative efficacy of CT and angiography in determining the etiology of third CNP becomes more apparent if patients are divided in this manner (Table 3).

Isolated Third CNP

This group comprised 31 patients: all patients from categories 1 and 4, one from category 2, and two from category 3. CT was performed in 30 of these patients. The neuroradiologic evaluation and the clinical disposition of patients with isolated third CNP is challenging because of the low yield of

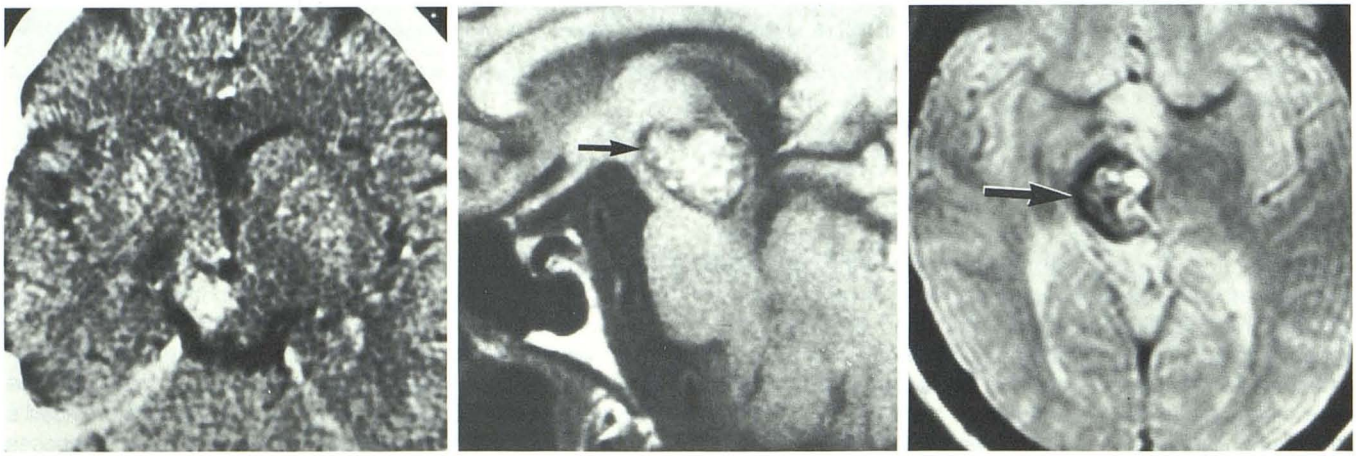


Fig. 7.—65-year-old woman with complete right third nerve palsy and left central facial weakness.
***A*, CT shows well-circumscribed contrast-enhancing lesion in thalamus extending into pretectal region of right midbrain.**
***B*, Sagittal T1-weighted SE sequence (TR/TE = 0.8 sec/17 msec) shows midbrain lesion with multiple punctate areas of hyperintense signal surrounded by rim of hypointense signal (*arrow*).**
***C*, Axial, mildly T2-weighted SE sequence (TR/TE = 2.5 sec/70 msec) at same level as *A* shows serpiginous area of hyperintense signal surrounded by peripheral rim of hypointense signal (*arrow*), compatible with hemosiderin from old hemorrhage within angiographically cryptic arteriovenous malformation confirmed by stereotactic biopsy.**

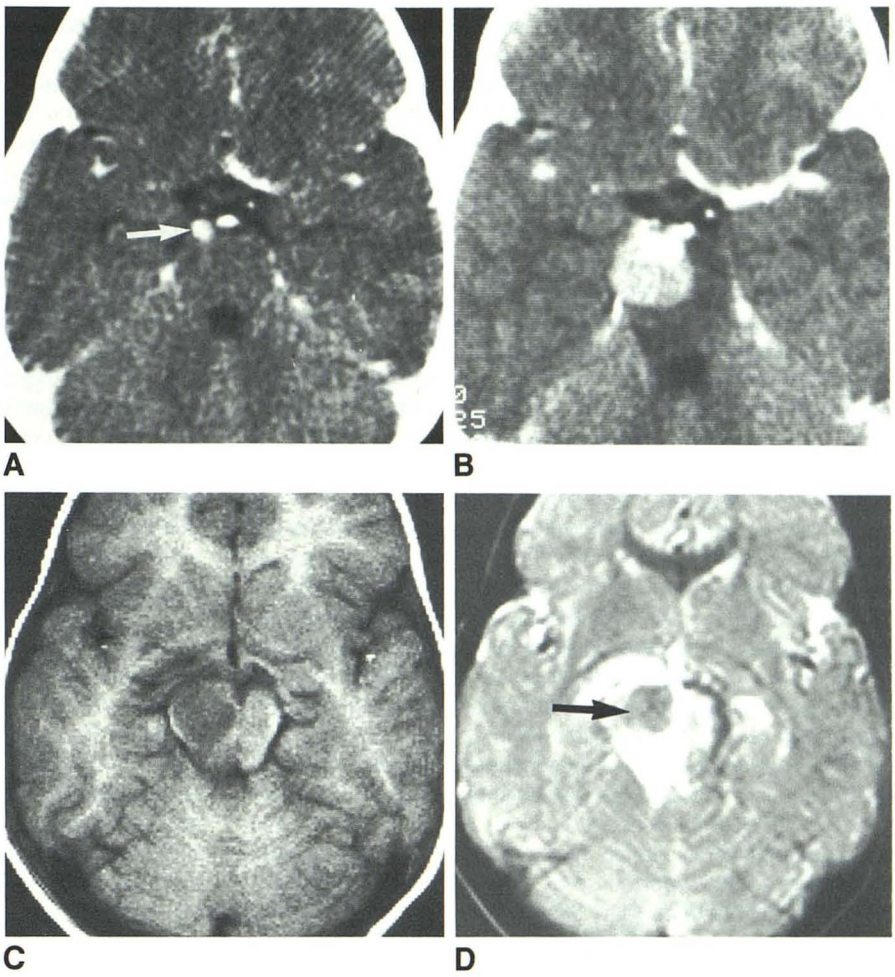


Fig. 8.—13-month-old boy with isolated complete right third nerve palsy.

***A*, Contrast-enhanced CT shows apparent extraaxial lesion (*arrow*) to right of basilar artery.**

***B*, Contrast-enhanced scan 2 months later shows marked enlargement of lesion. At this time the patient was hemiparetic on the left. CT could not clearly differentiate whether lesion was intra- or extraaxial.**

***C*, Intraaxial location of right midbrain lesion is well seen on T1-weighted SE sequence (TR/TE = 0.8 sec/17 msec) as area of hypointense signal.**

***D*, On T2-weighted SE sequence (TR/TE = 2.5 sec/140 msec), lesion has isointense signal (*arrow*) surrounded by hyperintense edema. Pathologic diagnosis was primitive neuroectodermal tumor.**

TABLE 3: Relative Efficacy of CT, Angiography, and Clinical Examinations in the Evaluation of Third Cranial Nerve Palsy

Study	Type of Cranial Nerve Palsy	
	Isolated (n = 31)	Complex (n = 32)
CT:		
Diagnostic	9	29
Nondiagnostic	21	3
Total	30	32
Angiography:		
Diagnostic	6	9
Nondiagnostic	8	7
Total	14	16
Correct clinical localization	29	30

high-resolution CT (nine of 30) in detecting the cause of the third CNP and the possibility of missing life-threatening PCA aneurysms. Careful history and close neuroophthalmologic monitoring are crucial in the management of these patients. The CT scans in 15 patients with isolated ischemic third CNP did not reveal any significant intracranial abnormality. Incidental CT findings were found in two category-1 patients (a posterior cerebral artery aneurysm at the peduncular segment in one patient and bilateral orbital varices in another). Selective carotid and vertebral angiography was diagnostic in six of 14 patients; all six had aneurysms in the circle of Willis and were from category 4 with pupillary involvement. The only incidental finding on angiography occurred in the myasthenia gravis patient; a posterior cerebral artery aneurysm was seen contralateral to the clinically suspected third CNP. In the other seven negative angiograms, the ipsilateral pupil was totally spared in four patients and partially spared in three.

Clinical localization of lesions responsible for third CNP based on history and neuroophthalmologic examination was incorrect only in the patient with myasthenia gravis and in the patient with an idiopathic third CNP. Myasthenia gravis does not truly fit the criteria of isolated third CNP, but it is included because we were misled by the presence of physiologic anisocoria, severe temporal headache, ptosis, and extraocular muscle dysfunction on the side contralateral to the incidental posterior cerebral artery aneurysm. Myasthenia gravis is one cause of pupil-sparing ophthalmoplegia and should always be excluded with a Tensilon test before invasive

neuroradiologic evaluation. The relatively high rate of correct clinical diagnoses in patients with isolated third CNPs is due to a combination of (1) careful documentation of the severity of pupillomotor dysfunction relative to the extraocular muscle palsy, (2) relating the quality and temporal sequence of retroorbital pain with pupillomotor dysfunction, and (3) careful observation for aberrant third nerve regeneration. If aberrant regeneration is present, a thorough investigation is indicated to exclude a subarachnoid compressive lesion, since this phenomenon is not seen in diabetic third CNPs [13]. Most PCA aneurysms point posteriorly, inferiorly, and laterally; therefore, an enlarging aneurysm often compresses the dorsomedial pupillary fibers located on the surface of the third nerve resulting in pupillomotor dysfunction. The high prevalence of pupil-sparing third CNPs in patients with diabetes is related to the relative sparing of the microvasculature supplying the periphery of the third nerve in contrast to the hyalinization and endothelial proliferation in the microvasculature supplying the center of the nerve [14].

In the classical presentation, isolated third CNPs secondary to PCA aneurysm and those secondary to microvascular infarction from diabetes/hypertension represent two ends of a spectrum in terms of the relative severity of pupillary involvement, but atypical cases from either category can overlap and mimic each other [15–21] (Table 4). In none of our five cases of PCA aneurysm was the pupil spared; however, in two recent series, 14% of PCA aneurysms had isolated pupil-sparing third CNPs at presentation [19, 22]. In our series, two of 16 patients with ischemic third CNPs had pupillary involvement; others have reported up to 23% of diabetic third CNPs with some degree of pupillary dysfunction [10, 23]. Therefore, the status of the pupil in and of itself cannot be the sole determinant as to whether an angiogram is indicated to exclude a PCA aneurysm. Given the low morbidity of angiography in experienced hands [24, 25], angiograms should be obtained in patients with isolated third CNPs who are young and have no clinical history of diabetes and/or hypertension. A small percentage of negative angiograms can be justified to detect PCA aneurysms that partially spare the pupil.

We found that CT was diagnostic in only nine of the 30 patients in this group (Table 3); therefore, our data suggest that despite the high detection rate for aneurysms arising around the circle of Willis diagnosed by thin-section dynamic CT scans as reported in the literature [26], the indication for CT is less convincing in patients with isolated complete third CNPs than in patients with complex third CNPs. In this subset of patients, angiography is necessary to exclude an aneurysm unless a nonvascular parasellar lesion has been identified on CT. If carotid angiography does not identify a PCA aneurysm, vertebral angiography should be performed, because up to 4% of aneurysms responsible for third CNPs have been reported arising from the vertebrobasilar system [27]. Proximal posterior cerebral artery aneurysms and dolichoectasia of the basilar artery also may be responsible for third CNPs [28, 29].

Complex Third CNPs

The complex third CNP group is composed of 32 patients—all the patients from categories 5 and 6 and one each from categories 2 and 3. The neuroradiologic evaluation of this group of patients can be tailored to the orbital, parasellar, midbrain, or supratentorial compartment, depending on the constellation of presenting signs and symptoms. Our data showed that contrast-enhanced CT was highly sensitive (29 of 32 patients) in identifying the potential cause of complex third CNPs (Table 3). The only exceptions were two post-trauma patients with nonspecific encephalomalacia. The only incidential CT finding was basilar artery dolicholectasia, seen in a category-2 patient with diabetic third CNP presenting with cerebellar dysfunction. In patients with complex third CNPs, selective carotid and/or vertebral angiography provided additional diagnostic information in nine of 16 patients (three giant cavernous carotid aneurysms, one basilar artery

TABLE 4: Classifications and Differential Diagnoses of Isolated Third Cranial Nerve Palsy (CNP) on the Basis of Clinical Features

Category No.	Extraocular Motor Dysfunction	Pupillary Involvement	Retroorbital Pain	Differential Diagnosis
1	Complete	Complete sparing	Severe, typically precedes third CNP	Diabetes in almost all cases
2	Complete	Partial sparing	Mild/moderate	Diabetes in most cases; PCA aneurysm and cavernous sinus lesions less likely
3	Partial	Partial or total sparing	Mild/moderate	PCA aneurysm likely; diabetes in a few cases; cavernous ICA aneurysm, cavernous sinus meningioma, and Tolosa-Hunt syndrome less likely
4	Complete	Complete pupillary dysfunction	Deep radiating pain concurrent with onset of third CNP	PCA aneurysm in almost all cases; cavernous sinus, sellar, and clival lesions less likely

Note.—PCA = posterior communicating artery; ICA = internal carotid artery.

aneurysm, one anterior communicating artery aneurysm, one parietal arteriovenous malformation, one basilar artery thrombosis, one trigeminal schwannoma, and one medial sphenoid wing meningioma). The seven nondiagnostic angiograms were in three midbrain/thalamic gliomas, two midbrain cryptic arteriovenous malformations, one tentorial meningioma, and one diabetic patient with cerebellar ataxia. All 16 patients had a varying degree of pupillary involvement.

The clinical history and neuroophthalmologic examination were as accurate as CT in predicting the location of pathology responsible for the complex third CNP (30 of 32 patients). In the two cases of incorrect clinical localization, one patient in category 5 presented with bitemporal hemianopsia, bilateral decrease in visual acuity, and relative pupil-sparing right third and sixth CNPs; the clinical diagnosis was posttraumatic chiasmatic syndrome. CT showed only nondisplaced fractures involving the petrous bone and the greater wing of the sphenoid on the right side, accounting for the right third and sixth CNPs. The second incorrect clinical localization was "brainstem glioma" in a category-3 patient with a giant basilar tip aneurysm and an incidental right PCA aneurysm.

Since either multiple CNPs or additional neurologic deficits were always present in patients with complex third CNPs, the nature of retroorbital pain and pupillary involvement was not relied on as heavily for clinical localization and for determining the need for angiography as in patients with isolated third CNPs. However, true pupil sparing should be distinguished from pseudo–pupil sparing; the latter occurs in two situations: (1) simultaneous sympathoparesis and parasympathoparesis (not uncommon in compressive lesions arising insidiously from the cavernous sinus [30]), as seen in one of our patients with a giant cavernous carotid aneurysm, and (2) aberrant regeneration of the third nerve leading to pupillary constriction associated with adduction, infraduction, or convergence.

On the basis of our experience and of other reports in the literature [20], the neuroradiologic evaluation of isolated third CNP is best guided by dividing the patients into four groups according to the relative deficits in the pupillomotor and extraocular muscle function (Table 4). Algorithms for the workup of all patients with third CNP are presented in Figure 9.

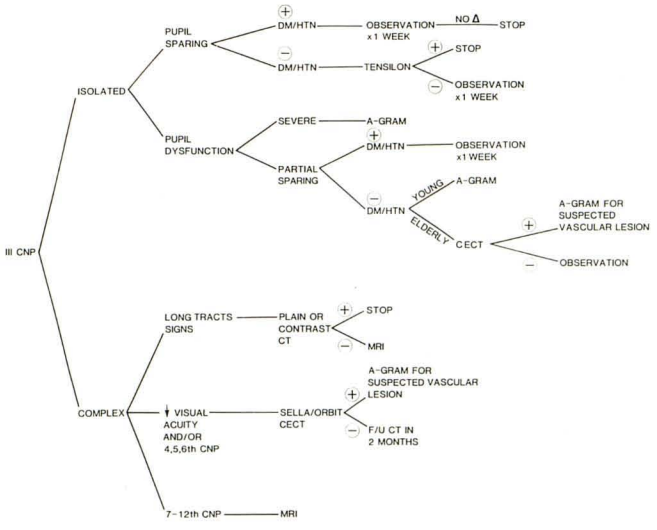


Fig. 9.—Algorithm for evaluation of third cranial nerve palsy (CNP). CECT = contrast-enhanced CT; DM/HTN = diabetes and/or hypertension; F/U = follow-up; MRI = magnetic resonance imaging; NO Δ = no progression; A-GRAM = angiogram.

Conclusions

1. In patients presenting with isolated third CNP, the CT yield is low (30%) unless diabetes and hypertension have been excluded; once those conditions have been excluded, the yield is 60%. Carotid angiography is indicated in all patients if the ophthalmoplegia is accompanied by any pupillomotor dysfunction. The vertebrobasilar system should be studied if the carotid angiogram is nondiagnostic.
2. The status of the pupil in and of itself cannot determine whether an angiogram is indicated to exclude an aneurysm. Careful ophthalmologic observation is mandatory to determine the logical sequence of radiologic evaluation.
3. Retroorbital pain alone is a nonspecific presenting symptom and has differential diagnostic value only if it is correlated temporally with the onset of third CNP and with the presence or absence of additional cranial-nerve deficits.
4. Contrast-enhanced CT is highly sensitive in detecting the etiology of complex third CNP; the yield was 90% in our series. A properly tailored neuroradiologic examination depends on the associated clinical findings.

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