Sequential Computerized Tomographic Appearance of Strokes

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SUMMARY Eighteen consecutive patients satisfying predefined clinical criteria for embolic strokes were prospectively studied by sequential computerized tomography (CT). Their findings were compared to CT scans obtained from patients presumed to have suffered thrombotic strokes. Our data reveal that the CT appearance of hemorrhagic infarction is likely to occur twice as frequently (22%) in CT scans of strokes presumed embolic than in those presumed thrombotic, where hemorrhagic infarction appeared at some time in 10% of the patients. No patient deteriorated with anticoagulation regardless of the CT appearance. In patients showing hemorrhagic infarction before anticoagulants, follow-up scans obtained after the administration of anticoagulants revealed resolution of the hemorrhagic aspect.

COMPUTED TOMOGRAPHY (CT) has become an indispensable tool in the investigation of patients with cerebrovascular accidents (CVA). While it is often possible to make a diagnosis of stroke on clinical grounds, CT is essential to eliminate non-ischemic etiologies of acute neurological deficits such as tumors. It is not yet certain however if CT can help distinguish between embolic and thrombotic ischemic infarction. While clinical guidelines in this regard are not absolute, the distinction is an important one since therapeutic intervention in thrombotic strokes is still largely limited to the removal or control of risk factors, such as hypertension, while anticoagulation is the suggested mode of treatment to prevent recurrences when it is likely that an embolus is the etiology of the ischemic episode.

While recent retrospective studies have favoured early anticoagulation in embolic strokes, the timing of anticoagulation is still controversial.

We evolved and adhered to clinical criteria that make an embolus a likely cause of a cerebrovascular accident. Eighteen consecutive patients (embolic group) who satisfied these criteria were studied by serial CT. Their CT findings were then compared to those found in ten patients identified retrospectively as suffering CVA's likely on a thrombotic basis (thrombotic group). These patients conformed to the same exclusion criteria as in the embolic group. The aims of this study were to identify possible CT scan features that may be helpful in confirming the clinical suspicion of cerebral embolism, and to detect any effect anticoagulation may have on the CT appearance.

Materials

Clinical Criteria for Embolic CVA

We adhered to the following criteria in determining the likelihood that a particular CVA was due to an embolus:

1. The presence of atrial fibrillation by history and/or on admission, proven by an electrocardiogram.

2. The diagnosis in hospital of a myocardial infarction within the previous 30 days.

3. The presence of a cardiomyopathy, idiopathic or alcoholic.

4. The presence of a prolapsed mitral valve confirmed by echocardiography, in the absence of other etiological factors of stroke.

5. The presence of a cardiac valve prosthesis whether or not the patient was already on anticoagulants.

Retrospective survey of thrombotic CVA

In selecting retrospectively patients whose CVA's were more likely due to thrombotic disease we relied on our hospital records. We identified patients admitted to our institution in the past two years with a clinical diagnosis of CVA. Their charts were then reviewed and 10 consecutive patients satisfying the following criteria were then selected.

1. No historical or clinical evidence of recent cardiac disease with at least one normal electrocardiogram in hospital.

2. Uninfused CT scans performed following admission and repeated at least once during the following three weeks.

Excluded from this study were patients with any of the following conditions:

1. An intracranial hemorrhage or tumor appearance on CT scan.

2. Patients suspected of suffering from bacterial endocarditis.

3. Patients with known or suspected contraindications to anticoagulation such as a history of peptic ulcers, a known coagulation defect, or a diastolic or systolic pressure above 100 or 180 mm Hg, respectively.

Methods

When a patient suspected of having an embolic CVA was admitted to hospital, a neurological consultation was obtained to confirm the diagnosis and adherence to the above criteria. The neurological exam was repeated weekly. Basic hematological and coagulation profiles, an electrocardiogram, a chest x-ray and a routine urinalysis were obtained within 24 hours of admission. An unenhanced CT scan was also obtained within 24 hours of admission and if possible repeated within 10 days and again during the third to fourth week following the CVA. This was done regardless of any treatment the patient may be receiving. Within 72...
hours of admission the patient received an echocardiogram.

On admission, these patients were randomly assigned to one of two anticoagulation groups: an early group all of whom were started on anticoagulation within 3 days from the CVA, and a late group anticoagulated no sooner than 7 days from the stroke. Once the absence of hemorrhage on the initial CT scan was ascertained, anticoagulation was started at the time assigned on admission if the patient did not deteriorate regardless of the appearance of the subsequent CT scans.

The CT scans obtained during the study were read by one of us (D.M.) who was unaware of the clinical history of the patient. Infarct size was estimated from a review of all the CT's obtained on any one patient and arbitrarily defined as small if the largest hypodensity noted on any CT was 1 cm or less in diameter, medium if between 1 and 3 cms, large if larger than 3 cms.

Results

Clinical data

Eighteen consecutive patients with CVA judged on the basis of the above criteria to be secondary to a cardiogenic embolus were accepted into the study (table 1). Eight patients were in the early anticoagulation group and ten in the late. Ten were female ranging in age between 83 and 52 years, and eight male ranging between 80 and 42 years. Fourteen patients were either known or discovered on admission to have atrial fibrillation and three were known to have suffered a myocardial infarct within the previous two weeks. One patient had previous cardiac infarcts, coronary artery bypass procedure and two episodes of systemic embolization in the previous year. In the group anticoagulated early, 2 of the infarcts were deemed large, 3 medium and 3 small, while in the group receiving late anticoagulation, the distribution in the same order was 6, 1 and 2. With two exceptions, all patients obtained an unenhanced CT scan on the day of admission. Ten patients on admission were on diuretics, nine were also on digoxin, three were on insulin, four were on beta-blockers and four were on no medication.

In the thrombotic group, table 2, nine of the ten patients were known hypertensives but their BP on admission was not beyond the exclusion criteria of 180/100 mm Hg. Three of these patients were also diabetic. Four were female ranging in age from 24 to 65 and 6 were male ranging from 45 to 83 years. Three of the patients, on decision of their physicians, were started on admission and thereafter maintained on anticoagulants. By CT, three of the infarcts in this group were large, 5 were medium and 2 were small. Eight of the patients were on antihypertensive treatment and 1 on insulin.

Anticoagulation was always started with heparin at doses sufficient to raise the partial thromboplastin time 1.5 to 2 times that of controls, and maintained there for three to four days before initiating coumadin.

Radiologic Data

Echocardiography, both M-mode and two dimensional, was performed in 16 patients in the embolic group. Eleven showed left ventricular dilatation and nine left atrial dilatation in addition. Two showed mitral stenosis, one showed atrial flutter and two were normal.

All the CT scans reported here were uninfused. Table 3 reveals the timing distribution of the CT's and the incidence of hemorrhagic infarction in them. A second CT was not obtained in 4 patients in the embolic group but not through a selection process: one died (see below), one left the hospital against our advice, and one patient refused to be subjected to a second scan as his first scan was normal and he was improving.

Hemorrhagic infarction was diagnosed on CT when curvilinear bands of increased density appeared around and inside a hypodense region of infarction giving the area a "mottled" appearance (fig. 1). None of the CT scans in the embolic group that was anticoagulated early showed this phenomenon, but 4 of the 10 patients in the group anticoagulated late did so, two showing it on the initial scan and two, in addition to one persistent hemorrhagic appearance, showing it on the second. Only one of the patients presumed to suffer from a thrombotic event showed an area of hemorrhagic infarction.

Clinical-Radiographic Correlations

One patient in the embolic group whose initial CT showed a hemorrhagic infarct and who was not anticoagulated, died 4 days following the CVA of cardiac and pulmonary complications. Otherwise no deterioration was noted in any patient. Of the remaining three patients whose second scans done five to ten days after CVA showed the hyperdense foci, none had yet been...
started on anticoagulants, but heparin was started within 1 day following this appearance. Repeat (third) CT scans performed in these three patients following institution of anticoagulation revealed total resolution of the hyperdense zones despite maintenance of anticoagulation (fig. 1).

No correlation between location or size of infarct and the appearance of hemorrhagic infarction could be

<table>
<thead>
<tr>
<th>Age/sex</th>
<th>Pertinent past medical history</th>
<th>BP on admission</th>
<th>ECG</th>
<th>Interval to anticoagulation (hrs)</th>
<th>CT, interval, days infarct location</th>
<th>Infarct size</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>A — Early anticoagulation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>77/M</td>
<td>chronic HBP</td>
<td>150/80</td>
<td>AF</td>
<td>36</td>
<td>1: L frontoparietal same 7:</td>
<td>large</td>
<td>obtunded</td>
</tr>
<tr>
<td>70/F</td>
<td>CAD, CHF, MI 2 years earlier, previous CVA</td>
<td>100/60</td>
<td>AF</td>
<td>70</td>
<td>2: previous infarct 10: new R occipital infarct evident</td>
<td>medium</td>
<td></td>
</tr>
<tr>
<td>83/F</td>
<td>previous CVA longstanding AF</td>
<td>130/60</td>
<td>AF</td>
<td>36</td>
<td>1: diffuse atrophy</td>
<td>small</td>
<td></td>
</tr>
<tr>
<td>42/M</td>
<td>none</td>
<td>100/70</td>
<td>AF</td>
<td>60</td>
<td>1: R frontal same 17:</td>
<td>large</td>
<td>echocardiogram reveals mitral stenosis</td>
</tr>
<tr>
<td>70/F</td>
<td>congestive cardiomyopathy</td>
<td>140/90</td>
<td>AF</td>
<td>36</td>
<td>1: normal 6: R parietal hypodensity 8: occipital hypodensity</td>
<td>medium</td>
<td></td>
</tr>
<tr>
<td>53/M</td>
<td>DM, hypertension MI — all 3y PTA</td>
<td>160/90</td>
<td>AMI</td>
<td>36</td>
<td>1: normal 8: occipital hypodensity</td>
<td>medium</td>
<td>CPK on admission 1748</td>
</tr>
<tr>
<td>74/M</td>
<td>angina claudication AF</td>
<td>100/60</td>
<td>AMI</td>
<td>24</td>
<td>1: R subcapsular hypodensity 20: normal</td>
<td>small</td>
<td></td>
</tr>
<tr>
<td>54/F</td>
<td>angina</td>
<td>170/90</td>
<td>AF</td>
<td>70</td>
<td>1: normal 9: lacune</td>
<td>small</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B — Late anticoagulation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>71/F</td>
<td>none</td>
<td>130/90</td>
<td>AF</td>
<td>1: L frontoparietal 6: HI 15: HI resolved</td>
<td>large</td>
<td>AC day 7</td>
<td></td>
</tr>
<tr>
<td>66/F</td>
<td>HBP, migraine AF</td>
<td>150/100</td>
<td>AF</td>
<td>1: L frontoparietal 7: same</td>
<td>large</td>
<td>AC day 13</td>
<td></td>
</tr>
<tr>
<td>62/F</td>
<td>DM, AF</td>
<td>125/75</td>
<td>AF</td>
<td>1: L frontoparietal 8: HI 19: HI resolved</td>
<td>large</td>
<td>AC day 9</td>
<td></td>
</tr>
<tr>
<td>65/M</td>
<td>HBP, DM</td>
<td>180/100</td>
<td>AF</td>
<td>1: HI</td>
<td>large</td>
<td>Pt did not get AC and died day 4</td>
<td></td>
</tr>
<tr>
<td>76/M</td>
<td>AF</td>
<td>130/80</td>
<td>AF</td>
<td>1: normal 13: L basal ganglia hypodensity</td>
<td>medium</td>
<td>AC day 13</td>
<td></td>
</tr>
<tr>
<td>52/F</td>
<td>Graves disease, nephrotic syndrome, AF</td>
<td>140/90</td>
<td>AF</td>
<td>1: R lacune 9: same</td>
<td>small</td>
<td>AC day 10</td>
<td></td>
</tr>
<tr>
<td>63/F</td>
<td>rheumatic fever, AF, osteoarthritis</td>
<td>160/90</td>
<td>AF</td>
<td>1: normal 18: normal</td>
<td>small</td>
<td>AC started day 11</td>
<td></td>
</tr>
<tr>
<td>63/F</td>
<td>DM, rheumatic fever, osteomyelitis</td>
<td>130/70</td>
<td>AMI</td>
<td>3: normal</td>
<td>small</td>
<td>AC day 17</td>
<td></td>
</tr>
<tr>
<td>57/M</td>
<td>angina, AC bypass, CVA</td>
<td>120/80</td>
<td>LVA</td>
<td>1: R temporoparietal hypodensity</td>
<td>large</td>
<td>Pt left AMA day 7</td>
<td></td>
</tr>
<tr>
<td>81/M</td>
<td>CHF, COPD</td>
<td>190/90</td>
<td>AF</td>
<td>1: HI 8: HI 28: resolved</td>
<td>large</td>
<td>AC day 9</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations used in Tables 1 and 2: AC anticoagulation, AF atrial fibrillation, AMI acute myocardial infarction, BCP birth control pills, BP blood pressure, CAD coronary artery disease, CHF congestive heart failure, COPD chronic obstructive pulmonary disease, DM diabetes mellitus, ECG electrocardiogram, HBP high blood pressure, HI hemorrhagic infarction, IC internal capsule, L left, MI myocardial infarct, OIWMl old inferior wall MI, R right, VBI vertebral basilar insufficiency.
made, although in the late anticoagulation group of embolic infarcts, all four such appearances occurred in large infarcts. However, this group had more large infarcts (60%) than in the other two categories.

**Discussion**

The intent of the present study was to compare the prospective evolution of the CT in presumed embolic CVA's with the CT appearance in a group of patients identified retrospectively as having suffered a thrombotic stroke.

Several investigators have reported the sequential CT appearance in cerebral infarction,8-11 but none have compared CVA's on the basis of their presumed etiology. We have attempted this by limiting our study to patients who on the one hand presented with a likely cardiac source for the cerebral embolus and on the other hand suffered from hypertension with or without diabetes and showed no likely cardiac source. Thus 14 of the patients in the group presumed to suffer from a cerebral embolus had atrial fibrillation on admission, which increases several fold the chances of suffering a CVA during the lifetime of the patient.12 Another three of these patients had suffered myocardial infarcts also known to be associated with increased incidence of cerebral infarction in the immediate period following the cardiac event.13 While such selection increases the likelihood that the CVA's in the patients in the embolic group were due to an embolus, it is impossible to be absolutely firm, since many of the patients in the embolic group clearly suffered from atherosclerotic vessel disease which may have led to thrombotic CVA's in some. It will be possible to investigate this point more adequately with digital subtraction angiography in the future. In addition to this shortcoming, the sizes of our patient groups were small and were compared by a non-uniform technique.

**Table 3**  Timing of CT Scans and Incidence of Hemorrhagic Infarction in Patients with Presumed Embolic or Thrombotic CVA

<table>
<thead>
<tr>
<th>Days post CVA</th>
<th>Embolic group</th>
<th>Thrombotic group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of patients</td>
<td>First CT 1-3</td>
</tr>
<tr>
<td>early</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>late</td>
<td>10</td>
<td>10(2)*</td>
</tr>
<tr>
<td>Thrombotic</td>
<td>10</td>
<td>10</td>
</tr>
</tbody>
</table>

*Numbers in brackets refer to the number of CT scans showing hemorrhagic infarction.
The CT appearance of hemorrhagic infarction is more likely to occur in embolic CVA's, a notion supported by the hemorrhagic tendency in pathological and CSF studies in embolic infarcts.

It is unlikely that these hemorrhagic infarcts would be confused with frank intracranial cerebral hemorrhages, the distinction being that the hyperdense zones are "mottled" in the former and solid and of very high density in the latter. In addition, none of our reported CT's show "luxury perfusion" since we avoided contrast enhancement. Not only is the exact significance of luxury perfusion still unclear but it seems to occur in cerebral infarcts without distinction of the etiology.

The distinction between hemorrhagic infarction and frank hemorrhage determines further therapy. Anticoagulation, as reviewed recently, is recommended in embolic strokes to decrease the incidence of recurrence, while obviously contraindicated in intracerebral hemorrhage. Its use in CVA's presumed thrombotic is still controversial. Our data, in this regard are revealing: not only can the CT show hemorrhagic infarction without the presence of anticoagulants, but anticoagulants do not seem to worsen this appearance, which continues to resolve in their presence (fig. 1). Thus, we feel safe in advising that if the initial CT scan shows no evidence of a frank intracerebral hemorrhage, anticoagulation may be maintained if there are no initial or subsequent clinical contraindications, with less emphasis on the evolution of the CT scan appearance.

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