Abstract: This study was carried out to determine whether certain clinical, laboratory, or radiological parameters predispose patients to develop FIRDA in acute situations. Charts of patients in whom FIRDA was detected on an EEG on hospital admission were reviewed. Demographic data, clinical history, physical findings, laboratory results and neuroimaging studies were recorded. Sixty-eight patients with a median age of 56 years were included. Chronic illness was present in 78%. Normal background activity was observed in only 17% of the cases. Epileptiform discharges were uncommon. Abnormal neurological findings were detected in over two thirds of patients. Renal function impairment was present in 34 patients, hyperglycemia in 22, and abnormal transaminases in 8. Cranial magnetic resonance imaging was abnormal in 15 of 17. Intrahemispheric lesions, particularly ischemic and hemorrhagic, were present in 10, and basal ganglia lacunae in 4. Computerized tomography was abnormal in 29 of 44. Most lesions were ischemic in nature. Brain tumors, hydrocephalus, and midline lesions were not detected. In conclusion, FIRDA is associated with encephalopathy and most patients in this series had a history of chronic systemic illness. Chronic, mostly ischemic structural brain lesions, may predispose some patients to develop FIRDA during acute metabolic derangement.

Key Words: FIRDA, EEG, clinical findings, metabolic disturbances

Introduction

Frontal intermittent rhythmic delta activity (FIRDA) is a frequent transient electroencephalographic finding in adults. The pathophysiological significance of FIRDA is unknown. Originally described by Cobb in 1945 (1), it was initially attributed to deep midline lesions and posterior fossa tumors (2,3). However, it has also been reported in association with third ventricle and pituitary tumors, subcortical lesions, hydrocephalus, cerebral edema, increased intracranial pressure, metabolic derangement and acute confusional migraine (4-7). The aim of this study was to determine whether certain clinical, laboratory, and radiological parameters predispose patients to develop FIRDA in acute situations.

Materials and Methods

Electroencephalographic recordings depicting FIRDA performed between January 1992 and January 1998 were retrospectively obtained from our computerized database at the Neurophysiology Laboratory at the Medical College of Virginia. Demographic data included age, sex, and race. Past medical and neurological history, clinical symptoms and signs, and neurological findings were recorded. Indications for current EEG, medications taken by the patient, EEG background activity, presence or absence of epileptiform discharges, and the state of consciousness during the recording were also analyzed.

Laboratory data included full blood count, serum electrolytes, glucose, kidney and liver function tests, calcium, magnesium, phosphorus, ammonia, creatine kinase, and blood gas analysis, cerebrospinal fluid (CSF) results and opening pressure. Blood, CSF, urine, and other culture results, urine toxic screen for drugs of abuse and for unknown drugs and urinalysis were also recorded. Neuroradiological studies included computerized tomography (CT) and magnetic resonance imaging (MRI) of the brain.

Results

Approximately 22,000 EEG recordings were performed during the specified period. FIRDA was detected in 147 cases. Sixty-eight medical records were available for analysis.
Sex ratio was equal, with a mean age of 56 years (range 1 year to 83 years). Race distribution: 44 (65%) black, 23 (33.8%) white, and one Asian patient. Most cases (63%) were admitted for neurological complaints. Significant past medical history was very frequent, occurring in 79.4% of the study group. Hypertension (34%), diabetes mellitus (32%), and renal failure (18%) constituted the most prevalent forms of chronic disease. Meningoencephalitis, previous hemorrhage, Parkinson’s disease, and epilepsy were the most common previous neurological insults. However, as a group, these constituted less than 20% of cases. In 15%, there was no previous neurological history, whereas in over 45% patients’ charts did not provide information on this subject.

Most patients (76%) were on chronic medications: Benzodiazepines (21%), insulin (19%), aspirin (16%), and ranitidine (15%) were the most prevalent.

The reason for hospital admission is shown in Table 1. Although many conditions led to hospitalization, seizures, stroke, and metabolic derangement constituted the core reason for admission in well over half of the patients.

Indications for EEG included rule-out seizures in 44 of 68 cases, altered mental status in 9, not specified in 9 cases, and status epilepticus in 6. Over 55% patients were awake during the recording, 10.3% were confused, 9.7% were lethargic/comatose, and in 25% their state was not specified. Among the 51 cases for which consciousness state was noted, 74.5% were awake, 13.7% were confused, and 11.8% were lethargic or comatose. EEG background activity was mild to moderately slow in 83% of the cases. Diffuse slowing was observed in the majority (69%). Normal wakefulness (posterior alpha rhythm) background occurred in 17%.

Epiptiform discharges occurred in only 4% of cases, who also had diffuse slowing in background activity.

Table 2 depicts the neurological findings in this series. Although some significant positive or negative neurological finding was detected in more than two thirds of cases, none of these findings were particularly prominent. Thirty-two percent of patients were neurologically normal on admission.

Renal function impairment was present in 34 patients (50%), hyperglycemia in 22, and abnormal liver enzymes in 8 cases. However, in the majority of these cases only one abnormal value occurred. Bacterial infections and hyperammonemia were not detected.

Cranial MRI was abnormal in 15 of 17 cases. Intrahemispheric lesions, particularly old ischemic and hemorrhagic ones, constituted the majority of the cases (n=10). They were diffuse in 3 patients, frontal in 4, parietal in 2 and occipital in one. Basal ganglia lacunae were detected in 4 patients and brainstem pathology occurred in one. CT was abnormal in 29 of 44 studies. Hemispheric pathology occurred in 22 cases: it was diffuse in 41%, frontal in 23%, and occipital in 14%. Periventricular white matter disease (n=8) and diencephalic lesions (n=6) were also common. Most lesions on MRI and CT were ischemic. There were no cases of brain tumors, hydrocephalus, or midline lesions.

**Discussion**

FIRDA is characterized by intermittent frontal delta runs of monorhythmic character and the delta frequency usually ranges from 1.5 to 2.5/second. The maximum of the activity lies over the frontopolar region, and the extent of spread varies considerably. There has been
some controversy about the genesis and clinical significance of FIRDA. The earlier literature emphasized the association of FIRDA and space occupying intracranial lesions. However, in later studies, non-tumoral etiologies of FIRDA were also reported, including toxic, metabolic, degenerative and infective encephalopathies, as well as cerebral infarction (4,7,8).

Schaul et al., in a study of 42 records with FIRDA found that FIRDA was a nonspecific finding and had no correlation with increased intracranial pressure (ICP)(8). In a study by Fariello et al., it was reported that 44% of patients with FIRDA had focal structural lesions, 34% diffuse structural and 22% had non-structural disease (7). They found FIRDA with both increased and decreased ICP. Hooshmand concluded similarly in his study that FIRDA was a nonspecific finding and is most likely to occur in acutely ill patients with changes in consciousness (4). Again, contrary to initial reports, Janati et al. showed that FIRDA can occur with strokes at any location and it does not correlate with midline shift (9). In another study comparing the EEG and computerized tomography, midline lesions were found only in a minority of patients with FIRDA (10).

In our series, FIRDA occurred more commonly in elderly patients with chronic hypertension, diabetes mellitus, or renal disease. Since there was no control group, the true importance of previous chronic illness in this population cannot be ascertained. However, only a minority of patients had no previous significant medical history.

EEG was obtained in all cases for acute neurological symptoms, most notably for suspected seizure activity. However, the neurological examination of these patients failed to reveal a prominent finding that could be associated with FIRDA. Although FIRDA was most common during wakefulness, it also occurred in a significant number of patients with encephalopathy and coma. The EEG background activity, however, showed slowing in the theta range in a majority of awake patients, suggesting some degree of encephalopathy.

Metabolic derangement was common, with renal impairment constituting 50% of abnormal laboratory values. Although hyperglycemia and abnormal liver function were also common, in most cases metabolic abnormalities occurred singly.

Finally, this study showed again that FIRDA is not associated with tumors, hydrocephalus, or deep midline lesions. At our institution, EEG recordings are obtained in most patients with acute or subacute neurological symptoms. Hence, FIRDA, if present, would have been detected in patients with brain neoplasm, and third ventricle lesions, since these patients would be unlikely to be hospitalized without undergoing at least one EEG recording.

Previous ischemic brain insults, particularly affecting the hemispheres, basal ganglia and diencephalon were the most prevalent neuroimaging findings in this study. Acute central nervous system lesions were rare, and probably do not correlate with FIRDA.

We conclude that FIRDA is associated with mild to moderate encephalopathy. Chronic, mostly ischemic, structural brain lesions may predispose some patients to develop FIRDA during acute metabolic derangement, such as uremia and hyperglycemia. FIRDA is not associated with EEG epileptiform activity and tumors, and deep midline lesions were not detected in this series of patients with FIRDA.

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