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Postictal Psychosis, a cause of secondary affective psychosis: a clinical description study of 77 patients

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Abstract

OBJECTIVE: Postictal Psychosis (PIP) is a severe complication occurring at least in 2% of patients with epilepsy. Since the 19th century, psychiatrists have reported the specificity of PIP presentation, but descriptions did not clearly distinguish PIP from after-seizure delirium. This study aimed to provide a precise description of psychiatric signs occurring during PIP, and improve recognition of PIP.

METHODS: We performed a review of clinical descriptions available in literature (48 patients), that we gathered with a retrospective multicentric case series of patients from three French epilepsy units (29 patients). For each patient, we collected retrospectively the psychiatric signs, and epilepsy features.

RESULTS: We found a high prevalence of persecutory (67.5%) and religious (55.8%) delusions, with almost systematic hallucinations (83.1%) and frequent mood disturbances (76.6%), especially euphoria. Severe consequences were not negligible (other-directed assault in 20.8%, self-directed in 13.0%). The type of delusion was associated with mood symptoms ($p=0.017$). Episode onset was mainly sudden/rapid (90.9%), its duration was mostly between one to 14 days (64.9%) and the response to antipsychotic medication was good. Disorder was recurrent in more than a half of the sample (57.1% of patients with at least 2 episodes).

CONCLUSION: Considering our findings, PIP resembles more to an affective psychosis, than a purely psychotic disorder. The presence of affective signs differentiates PIP from other psychotic comorbidities in epilepsy. Additionally, resemblance between PIP and psychotic manic episode might help to discuss links between epilepsy and bipolar disorder.

Keywords: « postictal psychosis » ; « epileptic psychosis » ; « case study » ; « semiology » ; « clinical neurology »

Introduction

Postictal psychosis (PIP) is a rare and severe psychiatric complication of epilepsy, occurring in roughly 2 % of patients with epilepsy (PWE)¹, but its incidence is probably underestimated². This disorder typically consists of a brief delusional episode with hallucinations occurring after a lucid interval following a cluster of focal seizures with or without secondary generalization¹. The most serious consequences of PIP are self- and other-directed aggressive behaviors³. Since 1861, psychiatrists have reported psychotic episodes with mystic delusion, hallucinations and excitement occurring after a seizure: the so-called “Grand Mal Intellectuel”⁴ by J. Falret or “epileptic clouded states” by H. Ey⁵, which would have corresponded to PIP. As psychiatric classification was not standardized, and video-EEG did not exist, “clouded states” or “grand mal intellectuel” could refer to non-homogeneous diagnoses, with no clear distinction between post-seizure delirium or confusion, PIP and non-convulsive status^{6,7}. In 1988, Logsdail and Toone studied PIP in 14 cases⁸ who had EEG-records during psychosis. They submitted criteria corresponding to the following definition: (1) episode of confusion or psychosis occurring immediately upon a seizure or within a week of the return to normal mental state; (2) episode having a minimum length of 24 hours and a maximum of three months; (3) mental status characterized by (a) clouding of consciousness, disorientation or delirium (b) delusions, hallucinations in clear consciousness (c) a mixture of (a) and (b); (4) No evidence of extraneous factors which might have contributed to an abnormal mental state : anti-epileptic drug toxicity, history of interictal psychosis, EEG evidence of non-convulsive status, recent head injury or alcohol/drug intoxication. In 1996, a study compared clinical differences between 30 PIP and 58 interictal psychoses (33 acute and 25 chronic)⁹. The authors found more religious and grandiose delusions associated with elevated mood in PIP, whereas interictal psychoses presented more schizophreniform traits. These studies suggested that PIP and interictal psychosis are two distinct entities and confirmed the specificity of clinical features in PIP. However, they did not provide a completely detailed psychiatric description⁹. Subsequently, studies on PIP mainly focused on risk factors, or pathophysiology, but not on clinical aspects. A recent survey study in France¹⁰ demonstrated that psychiatrists and neurologists had an imprecise knowledge about psychosis in epilepsy. Notably, distinction between postictal confusion and psychosis was not clear for almost 41% of participants¹⁰.

Aims of the study: We conducted a literature review of clinical descriptions, and a retrospective multicenter case series. We aimed to describe precisely psychiatric manifestations of PIP in order to highlight its clinical specificities. We also studied electroencephalographic and brain imaging

data. Considering the low prevalence of PIP, we collected the clinical descriptions from the literature and non-published medical reports from three epilepsy-expert centers. Moreover, literature case-reports mostly originated from epilepsy-expert centers, and homogeneity of the sample was assured using same exclusion criteria.

Methods

1. Selection of clinical descriptions

Our patient database was composed of clinical descriptions of cases available within literature and of medical reports from three Reference Centers of Epilepsy. In regard to published clinical descriptions, we performed research on PubMed, Google Scholar, and PsycInfo, with the terms: (« postictal psychosis » OR « post ictal psychosis » OR « post-ictal psychosis ») AND (« report » OR « case report » OR « case study » OR « case presentation »). We selected studies, written in English or French, published after the seminal study of Logsdail and Toone criteria in 1988 and until September 2020. Medical reports of PIP from three University Reference Centers of Epilepsy in France (Hôpital Central in Nancy, Hôpital Pitié-Salpêtrière in Paris, Hôpital Bretonneau in Tours) were also retrospectively collected.

We included patients diagnosed with PIP, according to the commonly used criteria adapted from Logsdail and Toone, defined by a psychotic state that develop within 1 week after a seizure¹¹. To guarantee the homogeneity of the sample, and avoid any doubt about diagnosis, we excluded patients with a history of chronic psychosis (possible recurrence triggered by the postictal state), patients with an episode shorter than 24 hours and no lucid interval (possible confusion), or patients with persisting fits during the psychotic state (possible non-convulsive status). Insufficient clinical descriptions were not included. We did not include patients aged under 16 years, because psychiatric clinical presentation in childhood can be different from adulthood. When patients had several episodes of PIP, repeated episodes used to be briefly described in reports and articles, we focused on the best described episode.

2. Clinical features

Clinical descriptions of PIP episodes were assessed by one of the authors (AT), and all uncertain features were reviewed by a second investigator (CH). According to the written description of the episode, available within the publication or the medical report, we collected biographical data as the gender, age at the first episode, and psychiatric symptoms as follows :

- (1) Delusion features: type of delusion (persecution, erotomania, grandiose, guilt, religion, reference, somatic, being controlled, misidentification), presence and type of hallucination, suspicious behavior, thought disorder (derailment or well-organized delusion), confusional signs or disorientation, mood features (euphoria/elation, depressed, mixed, blunted or neutral), mood-congruent delusion.
- (2) Severity signs: agitation level (severe if physical contention and sedation were needed / moderate if only sedation was needed / no agitation), aggressive behavior (self- or other-directed), presence of insight.
- (3) Chronology: presence and duration of lucid interval (in hours), mode of onset (sudden within 24 hours, rapid within one week, progressive over one week).
- (4) Evolution: psychosis duration, antipsychotic treatment and response, number of episodes.

Patients were excluded when four items or more (among those described above) were not available in the psychiatric description.

On the neurological part, we collected for each patient:

- (1) type of epilepsy and its localization (lobe and side), age at onset, number of years of evolution, risk factors for epilepsy, seizure frequency, presence of seizure cluster and secondarily generalization, drug-resistance.
- (2) Electroencephalography (EEG) during psychosis: presence or not of interictal epileptic abnormalities, side of abnormalities
- (3) Brain imaging data: normal or presence of a structural abnormality (including hippocampal sclerosis)

3. Statistical Methods

All statistics were performed with the R software version 3.6.0. We first checked the absence of significant differences between psychiatric and neurological reported data among published and non-published patients, in order to assess the presence of a possible publication bias. Descriptive analyses were based on the sample size for the independent variables: psychiatric signs, epilepsy classification, EEG and Brain Imaging. Neurological explorations were heterogeneous among the patients: stereoelectroencephalography, video-EEG monitoring or standard interictal EEG were available on a case-by-case basis. As epilepsy work-up was performed in epilepsy-specialized centers, we could classify patients into four reliable groups of epileptic syndromes: unifocal temporal (usually mesial temporal associated or not with more extended temporal epilepsy),

unifocal extra-temporal, multifocal and unclassified epilepsy (none of the patients fulfilled criteria for presumably genetic Generalized Epilepsy). Moreover, as brain imaging results were potentially heterogenous, we preferred to consider only two reliable groups: normal and abnormal imaging. Considering the low proportion of patients with ictal recordings for localization of epileptic focus (41 out of 77 patients, see Table 1), no statistical association between epileptic focus and psychiatric signs could be made. To study the association between the psychiatric variables, we used Fisher's exact test. Results of Fisher's test are presented in percentages. A value of $p < 0.05$ was considered as significant. Effect size of significant associations was estimated with Cramer's V calculation, and considered as low under 0.2, moderate between 0.2 and 0.4 and strong over 0.4.

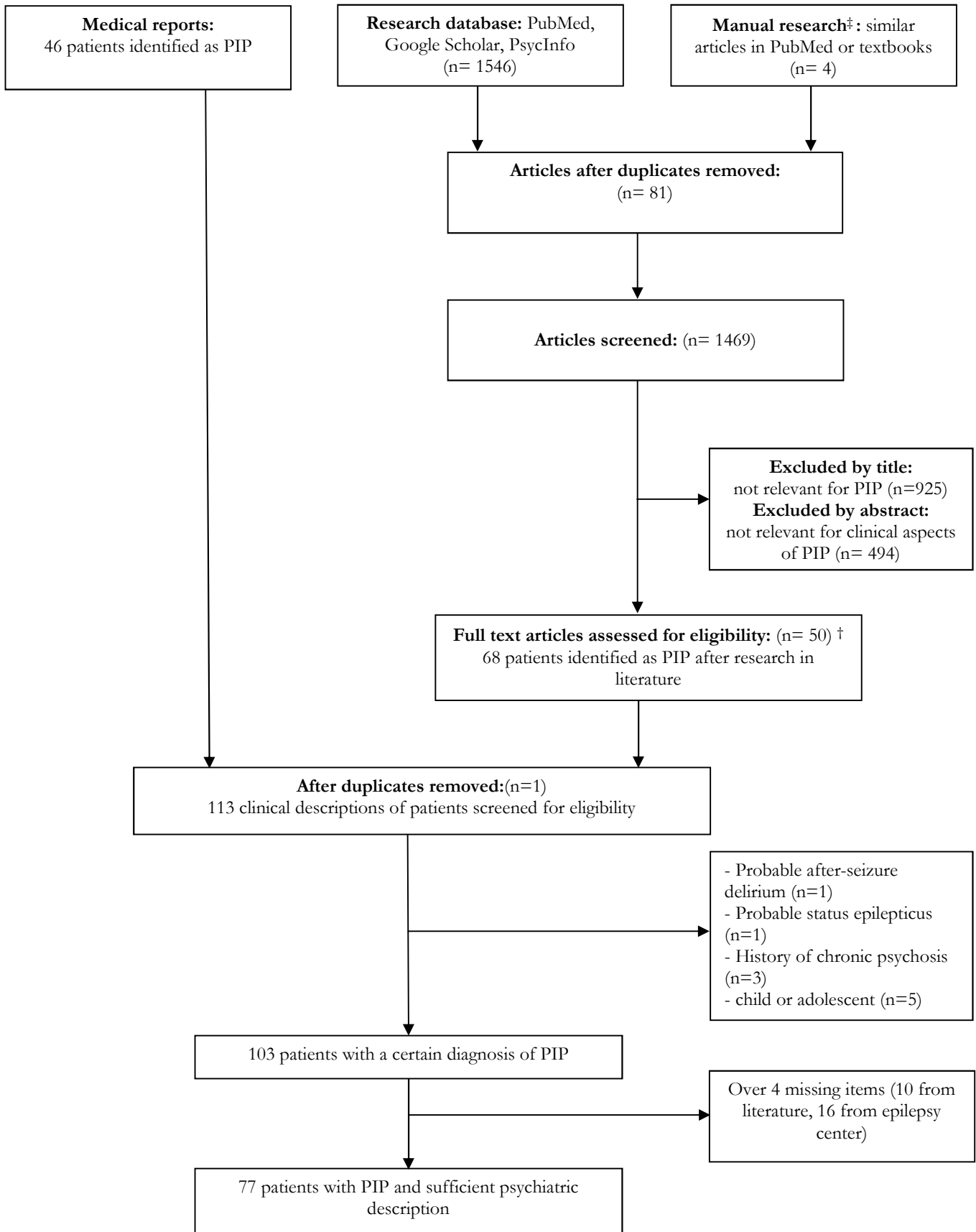
Results

1. Patient general description.

We identified 113 patients diagnosed with PIP, 77 patients were finally included in the study (5 presented exclusion criteria, 5 were aged under 16 years old and 26 were excluded for insufficient data). We collected 29 patients from three epilepsy centers (12 from Paris, 10 from Nancy and 7 from Tours) and 48 from international published literature^{3,8,12-40}. Sources of the data collected are described in Table 1. There was no significant difference in clinical symptoms between published and unpublished cases (except more delusion of being controlled in published reports). Males (n=43) and females (n=34) were almost equally distributed. Mean age at the first episode was 35.2 years (median=33, sd=9.3).

Table 1. Descriptive table of the sources of data collected for the present study

	Paris (n=12)	Nancy (n=10)	Tours (n=7)	Literature (n=48)
Type of source for psychiatric data	Medical reports and notes; nurses' notes	Medical reports and notes, nurses' notes, video recordings (when available)	Medical reports and notes	Manuscript, e-mail to authors (when response)
Type of source for diagnosis of epilepsy				
Prolonged v-EEG with ictal recordings	6 (50.0%)	7 (70.0%)	7 (100.0%)	20 (41.7%)
Prolonged v-EEG with interictal recordings	5 (41.7%)	3 (30.0%)	-	12 (25.0%)
Standard EEG with ictal recordings	1 (8.3%)	-	-	1 (2.1%)
Not detailed	-	-	-	15 (31.3%)
Type of EEG realized during psychosis				
Standard EEG	12 (100.0%)	5 (50.0%)	3 (42.9%)	23 (48.9%)
v-EEG	-	-	-	16 (33.3%)
SEEG	-	2 (20.0%)	-	2 (4.2%)
Not available	-	3 (30.0%)	4 (57.1%)	7 (14.6%)



(n: number of patient; EEG: electroencephalogram; v-EEG: video-electroencephalogram; SEEG: stereoelectroencephalography)

Figure 1. Flow chart of patient selection in the statistical study

(†: some paper provided descriptions for several patients; ‡: references obtained by personal research)

2. Psychiatric description of psychotic episodes

Missing data represented 5.9% for psychiatric signs. There was a total of 194 episodes, ranging from one to ten per patient (mean=2.5) and 44 patients (57.1%) presented at least two episodes. When patients had repeated episodes, subsequent episodes were shorter described, as similar to the first episode, within reports or papers. Lucid interval was clearly identified in 59 patients (76.6%), with a mean duration of 47.4 hours (median=32). Episodes began suddenly in 43 patients(55.8%) and rapidly (few days, less than one week) in 27 patients(35.1%). Delusion type was mostly mixed with several themes (median=2): especially persecution (n=52, 67.5%), religion (n=43, 55.8%). Hallucinations affected 64 patients(83.1%), were multimodal (median=2), especially auditory (n=49, 63.6%) and visual (n=40, 51.9%). Isolated visual hallucinations occurred in 8 patients(10.4%). Derailment was often associated (n=49, 63.6%), but confusional signs were infrequent (n=7, 9.1%). Monothematic and well-organized delusion occurred in 8 patients(10.4%). Affective state was often disturbed, either heightened (euphoric, or mixed n=43, 55.8%) or depressed (n=16, 20.8%). Delusion was mood-congruent in n=36(46.8%): 31 patients with elevated mood and 5 patients with depression. We found a significant slight correlation between the type of delusion and the mood level, with a higher proportion of religious and grandiose themes within euphoric patients (respectively 72.7% and 89.5%, $p=0.016$, $V=0.1$). Insight was mostly poor (n=72, 93.5%). Agitation concerned 63.7% of patients. We found aggressive behavior in 26 patients (33.8%): other-directed in 20.8% and self-directed in 13.0%. Severe consequences occurred in 10 patients(13.0%): 3 suicides, 1 stomach graft after caustic ingestion, 1 self-amputation of foot, 1 double-homicide, 1 nurse's wrist fracture and multiple child-stealing attempts. Duration was mostly short under 14 days in 50 patients (64.9%). Recovery was complete in 64 patients, including 51 who received medication. Descriptive analysis of psychiatric signs is presented in Table 2.

Table 2. Descriptive analysis of psychiatric signs of postictal psychosis in our sample of 77 patients.

	Cases (n)	Percentage		Cases (n)	Percentage
THEME			BEHAVIOR		
Persecution	52	67.5	Severe agitation	29	37.7
Religion	43	55.8	Moderate agitation	20	26.0
Grandiose	19	24.7	Calm	23	29.9
Reference	17	22.1	Other-directed aggr.	16	20.8
Being controlled	15	19.5	Self-directed aggr.	10	13.0
Guilt	12	15.6	Suicide/ sequelae	3/2	3.9/2.6
Somatic	7	9.1	Homicide/severe injury	1/4	1.3/5.2
Misidentification	4	5.2	<i>Insufficient data</i>	15	19.5
Erotomania	3	3.9	AFFECTIVE STATE		
<i>Insufficient data</i>	-	-	Euphoria / elation	25	32.5
HALLUCINATIONS			Mixed	18	23.4
Auditory	49	63.6	Depressed	16	20.8
Visual	40	51.9	Neutral	7	9.1
Somatic	17	22.1	Blunted affect	5	6.5
Olfactive	0	0	Mood-congruent delusion	36	46.8
Gustative	0	0.0	<i>Insufficient data</i>	7	9.1
<i>Insufficient data</i>	4	5.2	MODE OF ONSET		
OTHER FEATURES			< 24 hours (sudden)	43	55.8
Derailment	49	63.6	< 1 week (rapid)	27	35.1
Suspiciousness	36	46.8	> 1 week (progressive)	0	0.0
Well-organized delusion	18	23.4	<i>Insufficient data</i>	7	9.1
Disorientation / confusion	7	9.1	DURATION - RECURRENCE		
Insight (partial)	5	6.5	< 24 hours	6	7.8
<i>Insufficient data</i>	23	29.9	1 – 14 days	50	64.9
TREATMENT - RECOVERY			14 days – 1 month	13	17.1
Risperidone or Haloperidol	38	49.4	1 – 3 months	6	7.8
Chlorpromazine, Loxapine, Cyamemazine, Quetiapine or Olanzapine	14	18.2	Over 3 months	2	2.6
Other (i.e. amisulpride...)	5	6.5	Only 1 episode	33	42.9
None	13	16.9	≥ 2 episodes	44	57.1
Complete recovery	64	83.1	Total number of episodes ‡	194	-
<i>Insufficient data</i>	8	10.4	<i>Insufficient data</i>	-	-

(Some aspects of clinical symptomatology were not available posteriori: missing data represented 5.9% of all the database; n= number of patients except for ‡ where values are in a different unit detailed in the table; aggr. = aggression; PIP: postictal psychosis)

3. Neurological aspects : epilepsy type, EEG and Brain Imaging.

Epilepsy was unifocal in 63 patients (81.8%), mostly temporal (n=47) or frontal (n=6), and multifocal in 10 patients(13.0%). Focus was right-sided in 31 patients, left-sided in 27 patients and bilateral in 7 patients. Lobe and/or side data were missing in 12 patients. Epilepsy had lasted for 18.5 years (median:17, sd=9.1) and was frequently severe: mean of 6.0 seizures per month (median 4), secondary generalizations in 77.9% and drug-resistance in 67.5%. Seizure clusters affected 74.0% of patients, among whom clusters preceded psychosis. Most frequent risk factors for epilepsy were febrile seizures (n=11, 13.2%) and head trauma (n=11, 13.2%). For 14 patients, EEG during psychosis was not detailed, except the absence of epileptic status. When EEG patterns were detailed, they were usual interictal patterns: epileptiform (n=51, 66.2%), focal slowing (n=15, 19.5%) and normal (n=3, 3.9%). No forced normalization was mentioned. For 15 patients from literature, the comparison of EEGs between psychotic-state and non-psychotic state was described: 6 had an increase in interictal spikes^{8,14,21,29,33}, 2 a decrease²⁷ and 7 without modification^{8,13-15,25}. Brain imaging was normal in 32.5%, abnormal in 49.4%. Hippocampal sclerosis concerned 20.8% of all cases. Neurological aspects are presented in Table 3.

Table 3. Descriptive analysis of epilepsy type, EEG, and brain imaging in our sample of 77 patients

	Cases (n)	Percentage		Cases (n)	Percentage
TYPE OF EPILEPSY			RISK FACTOR		
<u>Unifocal epilepsy:</u>	63	81.8	Presence of a lesion:	12	15.6
Temporal:	47	61.0	Tumor	4	5.2
-Extended	29	37.7	Vascular	4	5.2
-Mesial	18	23.4	Inflammatory	0	0
Frontal	6	7.8	Others	4	5.2
Parietal	3	3.9			
Occipital	1	1.3	Febrile seizures	11	13.2
<i>Insufficient data (lobe)</i>	6	7.8	Head trauma	11	13.2
			Premature birth	5	6.5
<u>Multifocal epilepsy *</u>	10	13.0	Familial epilepsy	2	2.6
<u>Unclassified</u>	4	5.2	Alcohol or toxic use	2	2.6
<u>Side:</u>			<i>Insufficient data</i>	24	31.2
Right focus	31	40.3			
Left focus	27	35.1	SEVERITY SIGNS		
Bilateral	7	9.1	Presence of secondary generalization	60	77.9
<i>Insufficient data (side)</i>	12	15.6	<i>Insufficient data</i>	5	6.5
EVOLUTION †			Presence of seizures cluster	57	74.0
Seizure frequency (/month):			<i>Insufficient data</i>	12	15.6
Mean number of seizures	6.0	-	Drug-resistance	52	67.5
Median number of seizures	4.0	-	<i>Insufficient data</i>	10	13.0
<i>Insufficient data</i>	-	50.6	BRAIN IMAGING		
Duration of epilepsy at first PIP (years):			Normal (MRI or scan)	25	32.5
Mean	18.5	-	<u>Abnormal (MRI or scan) ‡:</u>	38	49.4
Median	17.0	-	Hippocampal sclerosis	16	20.8
<i>Insufficient data</i>	-	9.1	Tumoral lesion	7	9.1
EEG DURING PSYCHOSIS			Sequelae (trauma, surgery)	6	7.8
<u>Epileptiform</u>	51	66.2	Vascular lesion	2	2.6
Focal spikes	40	51.9	Inflammatory lesion	0	0
Rhythmic discharge	6	7.8	Other anomalies	7	9.1
Spike-waves	5	6.5			
			<i>Insufficient data</i>	15	19.5
<u>Slow activities</u>	23	29.9			
Focal	15	19.5			
Diffuse	7	9.1			
Normal	3	3.9			
<i>Insufficient data⁻¹</i>	14	18.2			

(* : 4 bi-temporal, 3 bi-frontal, 2 temporals + frontal, 1 temporal + occipital; n=number of patients, except for † where values are in a different unit detailed in the table; PIP: postictal psychosis; ‡: some patients had several lesions; Δ : EEG not detailed except the absence of epileptic status; PWE: patient with epilepsy)

Discussion

The main goal of this study was to characterize the clinical manifestations of PIP, as well as the epileptic aspects. Patients were distributed according to four epilepsy syndromes (unifocal temporal, unifocal extra-temporal, multifocal and unclassified epilepsy with bilateral epileptiform activity on EEG) and we distinguished normal and abnormal brain MRI. We studied 77 patients diagnosed with PIP, from medical literature or epilepsy expert centers. We excluded cases, with a persistent diagnostic doubt (probable non-convulsive status, or confusion, or other psychosis).

Clinical and psychiatric presentation of PIP

Onset of the disorder :

The age at first episode of PIP was relatively old (35 years in our sample, and around 37 within literature), that makes a significant difference with schizophrenia (around 26 years)⁴¹. Our results showed that PIP began suddenly or rapidly (within few hours or few days), approximatively two days of lucid interval after the last seizure. The lucid interval guarantees a clear-cut postictal period and the diagnosis of nuclear PIP¹¹. This interval was not systematically present in our sample, confirmed in literature⁴² (around one third of PIP without lucid interval). First, it could be explained by the fact that no witness could assert the presence of a clear lucid interval. Therefore, its absence might not be a criteria to invalidate the diagnosis of PIP. Secondly, some authors considered a larger concept of Postictal disorder with behavioral, mood or psychotic symptoms, containing numerous peri-ictal events, such as postictal mania, hypomania or, PIP, subacute postictal aggression or PIP without lucid interval¹¹.

Duration of episode :

The psychotic episode was globally short (under 14 days) and recovered after antipsychotic medication or spontaneously. The disorder was frequently marked by repeated episodes clinically identical in each patient. A previous study showed a mean duration of 10 days, and repetitive episodes kept the same duration⁴². Longer episodes tended to be associated with risk factors of psychosis (history of interictal psychosis, intellectual disability and family history of psychosis)⁴².

Psychiatric symptoms :

Clinically, the episode was characterized by a mixed-type delusion: persecutory, religious and grandiose. Affective symptoms, especially elevated mood, were very frequent. Neutral mood was relatively rare during PIP. Therefore, the mood could have constituted the core of the delusion, as suggested by the correlation between the mood and the type of delusion, or the proportion of

mood-congruent delusions, notably within euphoric patients. Mood disturbance, consistent with our series, constitutes the PIP specificity as compared to interictal psychosis of variable duration, the so-called schizophrenia-like psychosis⁹. As discussed in previous literature, the epileptic foci might play a role in the psychiatric symptoms, more precisely the link between temporal lobe epilepsy (TLE) and religious delusion,⁴³ or between TLE of the dominant hemisphere and psychosis⁴⁴. Nonetheless, associations between laterality of epileptic focus and type of psychiatric comorbidities are not systematically concordant^{45,46}, that may be explained by the low spatial resolution of surface EEG. Hallucinations also occurred as a main positive symptom of PIP, and affected several perceptions (i.e. auditory, visual and somatic). Indeed, the presence of visual hallucinations, and their terrifying content are described in literature, as a frequent feature of PIP^{4,47}. Regarding our results, visual hallucinations during PIP concerned half of patients, but it occurred less in the psychosis spectrum (prevalence of 15%, 21% and 27% among affective psychosis, first-episode psychosis and schizophrenia)⁴⁸. The delusion was mostly disorganized, with a high rate of thought derailment, that was not secondary to confusional state. Even though episodes had a complete recovery, the insight during psychosis was poor.

Associated to those traits, behavior was disturbed, with frequent manifestations such as highly agitated state and aggressive behavior, especially when the mood was heightened. Indeed, other-directed assault occurred at least once in one fifth of our patients and few committed suicide. Aggressiveness seemed to depend on the mood level and agitation, that were probably not independent. Regarding forensic psychiatry, epilepsy and violence have been described for two centuries (since Falret publications)^{4,3} dealing with the legal responsibility of PWE, but it has been debated more recently⁴⁹.

Epilepsy history and EEG :

The duration of the disease was long (around 20 years), its localization frequently focal, especially temporal lobe epilepsy without predominant laterality. Epilepsy was frequently very active with high seizure frequency, and often severe with presence of seizure clusters, secondary generalizations, and high rate of drug-resistance. Our findings are concordant with previous literature regarding clusters of seizures, generalizations and drug-resistance¹¹, but not for unifocal epilepsy. Previous literature provides arguments for bilateral independent ictal and interictal activities^{11,54}, as risk factor for PIP. In our study, patients were selected for the exhaustivity of the psychiatric data during PIP. Therefore, the potential lack of precisions for epilepsy features, or the heterogeneity of explorations, might explain this difference with previous findings. Brain

imaging did not highlight a specific etiology and was normal in roughly a third of the patients. EEG during PIP contained usual interictal abnormalities, that helped to differentiate from other epileptic psychosis, such as ictal psychosis or alternating psychosis. Indeed, when EEG shows continuous, more or less fluctuating epileptiform activity of focal origin, the diagnosis is a focal nonconvulsive status with ictal psychosis (i.e. frontal and temporal status could mimic PIP in some cases^{50,51}). Conversely, when the EEG is unusually normal, or seizures have completely ceased for at least one week, Forced Normalization and Alternating Psychosis⁵² must be considered.

PIP is a brief pleiomorphic affective and psychotic episode with behavioral disturbances, a major risk of recurrence and occurs in long lasting mostly refractory focal epilepsy. An early detection and specific treatment is mandatory to prevent violent behaviors⁵³. The differential diagnosis between other epileptic psychoses is essential, as treatment will differ⁵³. EEG can be a useful tool for classification and should be used by the clinician. Hence, in the presence of a psychotic episode with visual hallucinations lasting several days, an EEG should be performed to facilitate the diagnosis between epileptic status, psychiatric comorbidities of epilepsy, especially in the postictal period⁵⁴.

PIP, as an affective psychosis

According to our results, the presence of affective symptoms would be an important dimension of the syndrome. The association between elevated mood and post-seizure period is already reported as “organic euphoria” in literature about convulsive therapy in depressive disorders⁵⁵. Thus, there is a similarity of mood elevation in PIP and ECT-induced mania. Pathophysiology of ECT-induced mania remains unclear. However, clinically, the manic episode occurred within 24 hours after the treatment (following a kind of “lucid interval”) lasted several days and recovered spontaneously⁵⁵. ECT-induced mania is mostly seen in bipolar disorder⁵⁵. We might interrogate the association between epilepsy and bipolar disorder^{11,56} considering the similarities between PIP, ECT-induced mania and psychotic depression. Indeed, mood was mostly abnormal in our series, either elevated or depressed, and rarely neutral. Bipolar disorder and PIP are both recurrent episodic disorders. Moreover, studies revealed that family history of mood disorder, but not psychotic illness, is associated with a three fold increased risk of PIP⁵⁷. Some studies reported common neurobiological markers of bipolar disorder and epilepsy⁵⁸. In the same way, antiepileptic drugs constitute a pharmacotherapy for bipolar disorder and we cannot deny the resemblance of interictal dysphoric disorder and cyclothymia⁵⁹. A previous study compared manic episodes in epilepsy to those in bipolar I disorder: symptoms were similar but less severe and

more fluctuating in epilepsy⁶⁰ One could also interrogate the existence of different subtypes of PIP such as manic, depressive, or atypical episodes.

Limitations

The present work had several limitations. This is a retrospective uncontrolled case series, and it has a potential lack of precision for epilepsy data. This design is nevertheless suitable to our objective⁶¹, that was to study clinical descriptions of a rare and underrecognized syndrome. PIP does not correspond to a specific diagnosis code, often occurs after the epileptology-unit discharge and is brief, so that this syndrome could be easily unrecognized or undiagnosed. Therefore, we could not perform a second psychiatric examination to confirm the diagnosis and the symptoms. But the current design allowed us to study more cases, and our exclusion criteria might have eliminate uncertain PIP. Our cases series was collected both from hospital reports and from literature, and this could constitute a selection bias and heterogenous psychiatric evaluations. We found no notable difference in clinical symptoms between published and unpublished cases. Psychiatric assessments of patients were made by different clinicians, from different centers. However, patients from literature and reports mostly originated from epilepsy-expert centers, used to assess psychiatric comorbidity in epilepsy.

To our knowledge, this is the largest case series of PIP and the first systematic review to provide a multicentric and international exhaustive description of delusion in PIP. Our results presented an external validity and were concordant with previously described clinical aspect and epileptic syndromes⁶².

Contributors: AT, CH, BdT had the idea for the study and wrote the initial analysis plan. AT, OA, CH did the data analysis. AT produced the figures. AT, CH, BdT wrote the first draft of the report, and all other authors (OA,SD,LM) contributed to editing and commenting on the final version.

Authors confirm that they have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Ethical standards: The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees, and with the Helsinki Declaration of 1975, as revised in 2008. The design was retrospective, we collected data that were

already produced. This study did not contain personal data, that could identify the patients. All adult participants, from the three epilepsy centers, provided written informed consent for scientific use of their medical data after anonymization.

Availability of data and materials: The datasets used and/or analysed during this study concerned some medical data from reports and are available from the corresponding author on reasonable request.

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