INTRODUCTION

Epilepsy is a heterogeneous condition with numerous etiologies including genetics, cerebral trauma, toxic exposures, vascular diseases, infections, metabolic abnormalities, malformations and neoformations. Among the last ones, pituitary tumors (PT) are exceptionally responsible for convulsions, except when they are very large involving the suprasellar area and the nervous system. In English literature apart from anecdotic cases, there is only one report about epilepsy frequency in male macroprolactinomas. Our aim was to analyze generalized seizures and conditions under which seizures appear and disappear in men harboring macroprolactinomas or somatolactotroph adenomas.

MATERIALS AND METHODS

In this retrospective study, we analyzed 90 subjects, collected between 1992 and 2012, harboring macro-adenomas (>1 cm) secreting prolactin (PRL) (n = 82) or both PRL and growth hormone (n = 8) to seek symptoms of generalized seizures. We took into account family and personal medical history, clinical examination, routine and hormonal analyzes, and radiological assessment based on cerebral magnetic resonance imaging. Results: Between 1992 and 2012, we collected eight cases (8.9%): Seven were hospitalized for recent generalized seizures; one had epilepsy after conventional radiotherapy given in 1992 because of neurosurgery failure and resistance to bromocriptine. Their median age was 33.75 years (22-58), median PRL was 9,198 ng/ml and median tumor height was 74 mm (41-110). The temporal lobe was invaded in six cases. After tumor reduction, epilepsy disappeared and never relapsed after a follow-up varying between 1 and 20 years. Conclusion: Epilepsy, which is a life-threatening condition, can be the first presentation in men with prolactinomas or somatolactotroph adenomas, especially those involving the suprasellar area, and the brain. Convulsions can also appear after radiotherapy. That one should be avoided, if possible, before tumor reduction by surgery or medical treatment.

Key words: Epilepsy, large prolactinomas, male, radiotherapy
testosterone, follicle stimulating hormone (FSH), luteinizing hormone (LH), thyroid stimulating hormone (TSH) and free thyroxin (FT4). Radiological assessment was based on cerebral computed tomography scan (CT scan) and magnetic resonance imaging (MRI). After a significant reduction in their PT, they were re-questioned and re-explored on the neurological side and then we tried to stop progressively their antiepileptic drugs. The follow-up varied from 1 to 20 years.

**RESULTS**

In this study, we found eight subjects who experienced generalized seizures (8.9%). Before seizures all were complaining of headaches, decreased visual acuity and libido. Seven were sent to our department for generalized epilepsy related to large PT after exclusion by the neurologists of cerebral malformations and other epileptic etiologies such as familial, metabolic, traumatic and infectious causes. In the eighth case, tonic-clonic seizures appeared after conventional radiotherapy given in 1992 for a huge prolactinoma resistant to dopamine agonists.

Among the seven spontaneous tonic-clonic seizures, six were related to macroprolactinomas and one to a mixed adenoma secreting PRL and GH.

The median age of the eight persons was 33.75 years (22-58) and all their tumors were giant (height ≥ 40 mm) invading the suprasellar area and or the brain. Median tumor height was equal to 74 mm (41-110). PRL average (after systematic dilution) was equal to 9,198 ng/ml. The temporal lobe was invaded in six cases (75%) as in the Figure 1.

For the outcome, after tumor volume reduction [Table 1] observed after bromocriptine intake alone (n = 5), bromocriptine plus somatostatin’s analogs (n = 1) and after radiotherapy plus cabergoline and bromocriptine (n = 1), epilepsy disappeared and epileptic drugs were stopped in all cases. Seizures never reappeared for a follow-up varying between 1 and 20 years.

**DISCUSSION**

Epilepsy is a heterogeneous disorder with numerous etiologies. The mechanism can be genetic, metabolic, structural, infectious and tumoral.[1] Concerning tumors, seizures are a common complication in large intracranial lesions and clinical symptoms vary according to tumor localization.

Seizures are extremely rare in people with PT. According to Kawasaki et al., seizures secondary to PT are exceptional as they account for only 4% among all intracranial tumors causing seizures.[3] Convulsions appear when the tumor invades the suprasellar area and/or the nervous system creating an epileptic area.[3,4] Deepak et al.[4] found that 6/29 (20%) patients harboring prolactinomas with suprasellar expansion suffered from epilepsy at diagnosis. Most of them were men and had a temporal crisis i.e. experiencing visual, olfactory and auditory hallucinations and psycho sensory features such as sensation of already seen “déjà vu” or never seen “non vu” or derealization.[2] For our

<table>
<thead>
<tr>
<th>Patients</th>
<th>Natremia (135-145 meq/l)</th>
<th>Calcemia (85-110 mg/l)</th>
<th>Glycemia (0.7-1.10 g/l)</th>
<th>MRI</th>
<th>Tumor size before treatment (mm)</th>
<th>Tumor size after epilepsy disappearance (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N°1: Prolactinoma</td>
<td>139</td>
<td>96</td>
<td>0.76</td>
<td>Yes</td>
<td>68×50×50</td>
<td>45×40×27</td>
</tr>
<tr>
<td>N°2: Prolactinoma</td>
<td>140</td>
<td>92.5</td>
<td>0.93</td>
<td>Yes</td>
<td>50×68.5×46</td>
<td>25×34×34</td>
</tr>
<tr>
<td>N°3: Prolactinoma</td>
<td>143</td>
<td>90</td>
<td>1.05</td>
<td>Yes</td>
<td>110×60×78</td>
<td>60×55×48</td>
</tr>
<tr>
<td>N°4: Prolactinoma</td>
<td>142</td>
<td>98</td>
<td>0.89</td>
<td>Yes</td>
<td>41×27×34</td>
<td>18×15×30</td>
</tr>
<tr>
<td>N°5: Prolactinoma</td>
<td>139</td>
<td>94</td>
<td>0.84</td>
<td>Yes</td>
<td>65.6×97.1×62</td>
<td>31×55×30</td>
</tr>
<tr>
<td>N°6: Prolactinoma</td>
<td>137</td>
<td>99</td>
<td>0.85</td>
<td>Yes</td>
<td>61×63×45</td>
<td>12×30×14</td>
</tr>
<tr>
<td>N°7: Somatolactotroph adenoma</td>
<td>140</td>
<td>107</td>
<td>0.89</td>
<td>Yes</td>
<td>80×100×70</td>
<td>23×47×37</td>
</tr>
<tr>
<td>N°8: Prolactinoma</td>
<td>140.6</td>
<td>100</td>
<td>0.75</td>
<td>Yes</td>
<td>41×59×38</td>
<td>21×38×11</td>
</tr>
<tr>
<td>N°9: Prolactinoma</td>
<td>138</td>
<td>89</td>
<td>0.76</td>
<td>Yes</td>
<td>50×55×62</td>
<td>18×28×25</td>
</tr>
</tbody>
</table>
group, generalized epileptic seizures were observed in 8 of 90 (8.9%) men harboring macro adenomas secreting PRL (82 pure prolactinomas and 8 somatolactotroph adenomas). If we consider only tumors superior or equal to 4 cm (n = 46) our percentage will rise to 17.3%! This percentage is slightly lower than Deepak’s.[4] Our frequency is probably under estimated as we did not take into account partial seizures and we did not do a systematic electro-encephalography to all our patients. Epileptic seizures are apparently due to mass effect on the brain system as convulsions are described only in people with very large PT or those harboring pituitary metastasis invading the suprasellar area.[8] But, a fortuitous association with a mrioadenoma or an isoadenoma is not impossible. To our knowledge high PRL or GH concentrations are not inocriminated in epileptic status, but after epilepsy crisis hormones influenced by stress such as PRL, GH, cortisol, and even LH and FSH can raise.[7]

It is also interesting to note that seizures may occur in patients harboring huge tumors which are treated by dopamine agonists.[8] In such cases a very rapid reduction in tumor volume would cause an unintended movement of brain structures responsible for epileptic seizures.[8] Conventional and even gamma knife radiotherapy is another cause of epilepsy in people with large prolactinomas or other PT.[9] Radiotherapy is generally aggressive for the brain as it can be responsible for radio-necrosis, gliomas or a mere change of the mesial temporal lobe mimicking gliomas.[9] Risks for inflammation and/or hemorrhage in PT and the brain are also increased by radiation as reported by some authors in prolactinomas[9] non-functioning adenomas[9] and somatotropinomas.[9,10]

In some exceptional situations, generalized seizures may reveal a PT as in seven of our cases. This situation traduces a very late diagnosis or a rapid progression of the tumor compressing cerebral structures. In our patients, convulsions were observed only in invasive prolactinomas and somatolactotroph adenomas deemed to be the largest PT. Large pure somatotroph adenomas can also induce seizures in animals[11] and human beings.[1,2]

Epilepsy secondary to PT is usually resistant to symptomatic treatment by antiepileptic drugs[11] but responds to medical treatment that reduces PT, even if tumor reduction is partial as observed in our study, and by Deepak et al.[4] Total resection of the tumor when possible and/or dopamine agonists for pure prolactinomas and mixed adenomas avoid recurrence of the life threatening seizures, lead to control and even recovery from epileptic crisis as we observed it. Similar results were observed by Castero Cabezas et al.[12] in somatotroph adenomas invading temporal lobes.

**Conclusion**

Epilepsy, which is a life-threatening condition can reveal prolactinomas in men and mixed pituitary tumors, especially giant ones. Convulsions can also appear under aggressive treatment such as radiotherapy. That one should be avoided, if possible, before tumor reduction by surgery or medical treatment.

**References**