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(CASE REPORT)

Craniopharyngioma in children: Report of three cases and review of the literature

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Abstract

Craniopharyngioma is a rare benign epithelial tumor, originating in the pituitary stem or pituitary gland and developing in the sellar and / or suprasellar region. Of embryonic origin, craniopharyngiomas are considered to develop from epithelial remains of Rathke's pouch. It affects children as well as adults. All ages combined, craniopharyngiomas represent between 3 to 4% of intracranial tumors worldwide, or 0.5 to 2 new cases per year and per million inhabitants. In children, they represent 10% of all intracranial tumors with a peak frequency between 7 and 13 years and a predominance of men. Although benign, this tumor remains a serious pathology because of the frequent visual, endocrine, neuro-intellectual sequelae and the risk of recurrence that it entails, involving the visual and vital functional.The management of this pathology is multidisciplinary and involves several modalities such as surgery, radiotherapy and medical treatment of hormonal deficits very often associated.

We report in this article three cases of boys aged 9, 10 and 12; treated for symptomatic craniopharyngiomas with a favorable clinical and radiological outcome after partial surgical excision and adjuvant external radiotherapy. The aim of this article is to review the epidemiological, diagnostic, therapeutic and evolutionary aspects of these benign tumors of the sellar and / or suprasellar region, with an emphasis on the interest of radiotherapeutic treatment.

Keywords: Craniopharyngioma; Child; Radiotherapy; Senegal

1. Introduction

Craniopharyngiomas are benign epithelial tumors, developing from the pituitary stem or pituitary gland in the sellar and / or parasellar region. Its worldwide incidence is 0.5 to 2 new cases per million inhabitant and represents 18% of suprasellar tumors in children and 55% of suprasellar tumors [1]. There are two histological types; the papillary type and the adamantine type which is found mainly in children with a prognosis similar to these two entities. Due to the origin and position of this tumor, the clinical picture may associate, to varying degrees, endocrine disorders, ophthalmologic disorders, signs of intracranial hypertension and related focal neurologic signs [2]. The management of craniopharyngiomas in children is multidisciplinary, associating surgical excision; radiotherapy and medical treatment of deficits [3].

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2. Patient and observation

2.1. Observation 1

9-year-old MS boy, with no particular pathological history, who had presented chronic headaches and left proptosis for 10 months. Three months before the consultation in neurosurgery, the symptoms worsened with a decrease in bilateral visual acuity and a left purulent tearing without sensitivomotor deficit. On admission, the examination objectified a patient with a clear conscience (Glasgow score = 15/15), a left exophthalmos with purulent secretions, a reactive right pupil; a decrease in visual acuity rated 4/10 on the right and 2/10 on the left without sensory and motor deficit. A brain CT scan with injection of contrast product is performed. It shows a significant expansive process in intra and supra sellar measured at 70 x 57 x 52 mm with a solidocystic component with exophthalmos left grade III very suggestive of craniopharyngioma. A few bubbles of intra-lesional pneumencephaly were noted with infiltration of the walls of the cavum delimiting foci of necrosis (figure 1, AB).

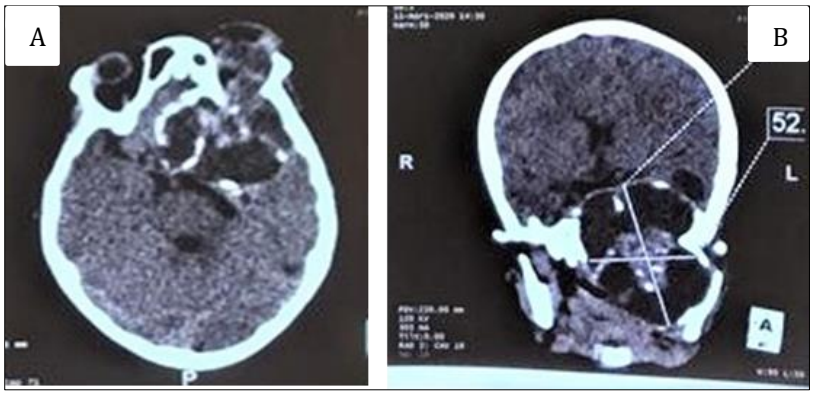

Figure 1 CT images showing an intra and suprasellar tumor process: A (axial slice); B (coronal cut)

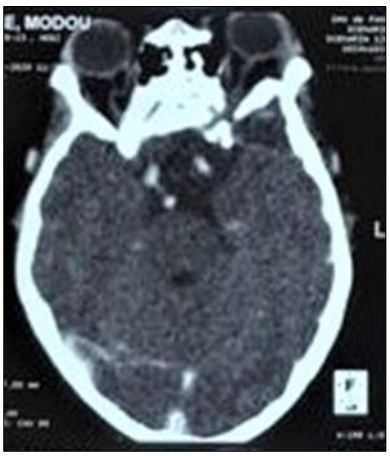

Figure 2 Axial section of a brain CT after surgery showing a tumor residue

An indication of resection of the craniopharyngioma by endoscopic route was made, and carried out with simple operative consequences without incident. The anatomopathological examination of the operative part of this surgery with invaded macroscopic margins (R2) confirms a craniopharyngioma of type adamantine or pituitary adamantinoma. A control postoperative brain scan found a residue of the lesion of 45 x 26 mm with grade II left proptosis (Figure 2). Adjuvant treatment with external radiotherapy using a three-dimensional conformational technique (RC3D) with multiple energy beams 6 to 10MV has been indicated and performed. The dose of 54Gy in classic fractionation of 2Gy per session was used and dosimetric planning made it possible to obtain a treatment plan covering the target volumes according to ICRU 50 with respect for the dosimetric constraints on the organs at risk (Figure 3). The tolerance of radiotherapy was good. The evolution was marked by a regression of the clinical symptoms, namely the headaches, the left exophthalmos; an improvement in visual acuity on the right without improvement on the

left. The follow-up brain CT scan 6 months after radiotherapy showed a centimetric area of lesion surrounded by areas of changes (figure 4). At 14 months after radiotherapy, the patient presented no persistent symptoms apart from the drop in visual acuity on the left, rated at 4/10.

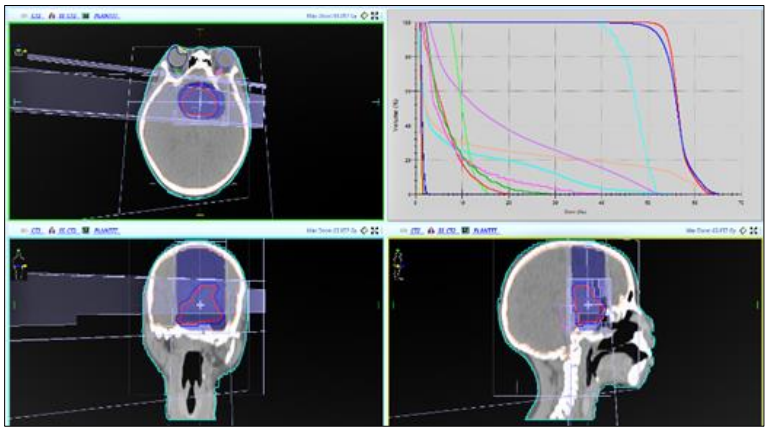

Figure 3 RC3D treatment plan with placement of treatment beams and dose volume histogram (HDV)

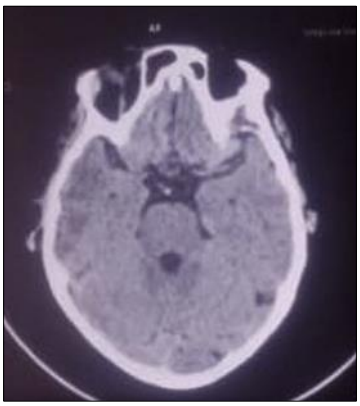

Figure 4 Axial section of a radiotherapy 6-month cerebral CT scan showing an area of lesion with areas of rearrangement

2.2. Observation 2

AS, 10-year-old boy, with no particular pathological history, who presented for 4 years morning headaches of occipital site and chronic course. Six months before the consultation in pediatrics then in neurosurgery, the symptoms worsened with vomiting and convulsive seizures associated with visual disturbances ranging from reduced visual acuity to bilateral blindness and generalized apathy. On admission, the examination noted a patient with a clear conscience (Glasgow score of 15/15), moderate intracranial hypertension syndrome, clinical cushing syndrome and failure to thrive. A brain scan with injection of contrast product is performed. It shows an important supra sellar expansive process with a solido-cystic component with macros calcifications in contact with the brainstem posteriorly and invading the optic chiasm plane in favor of a craniopharyngioma (figure 5, CD). The dosage of Insulin Growth Factor 1 (IGF1) was low at 76ng / ml and the growth hormone-stimulating insulin test (HGI) revealed growth hormone (GH) deficiency as well as previous insufficiency. Pituitary on the thyrotropic and corticotropic axis supplemented by 50 µg / d of Levothyrox and 20 mg / d of hydrocortisone associated with diabetes insipidus under desmopressin acetate. An indication of excision of the craniopharyngioma by craniotomy was made and carried out with simple postoperative procedures. Anatomopathological examination of the operative part of this surgery with invaded macroscopic margins (R2) confirms an adamantine-type craniopharyngioma. Adjuvant treatment by external radiotherapy using a three-dimensional conformational technique (RC3D) with multiple beams of energy 6 to 10MV a been carried out. The dose of 54Gy in classic fractionation of 2Gy per session was used and dosimetric planning made it possible to obtain a treatment plan covering the target volumes while respecting the dosimetric constraints on the organs at risk (Figure 6). The evolution was marked by a regression of the clinical symptoms, namely intracranial hypertension and hormonal

disorders with medical treatment. At 12 months after radiotherapy, the patient had no symptoms other than bilateral blindness which persisted.

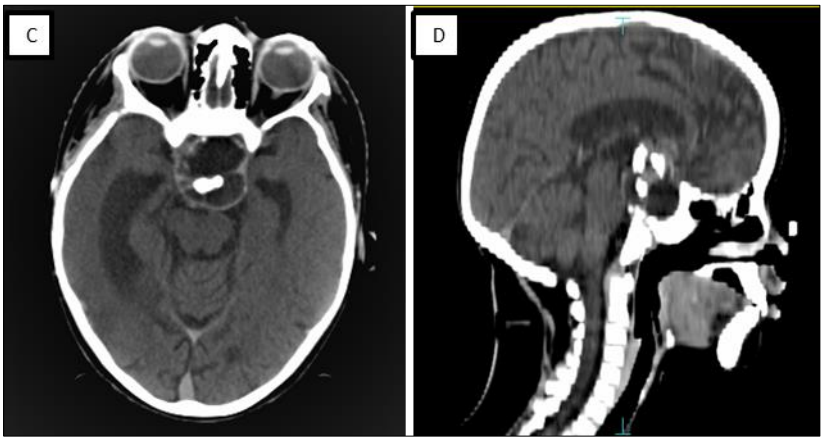

Figure 5 CT images showing a supra sellar expansive process with a solido-cystic component and macros calcifications: C (axial slice); D (sagittal cut)

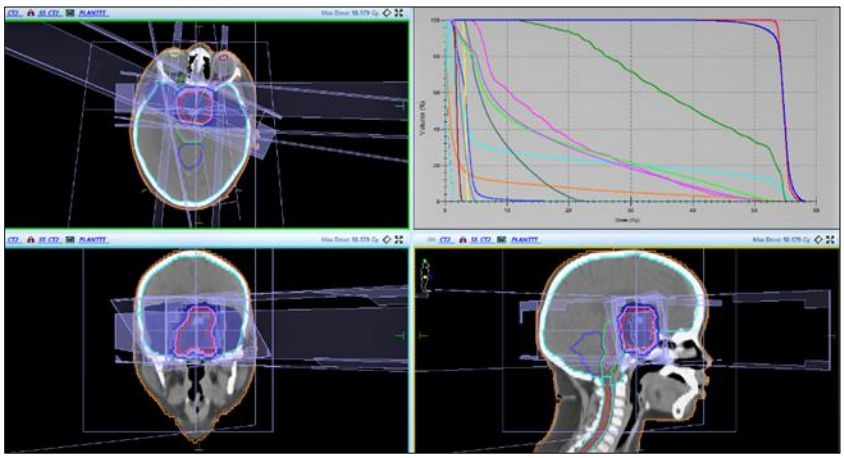

Figure 6 RC3D treatment plan with placement of treatment beams and dose volume histogram (HDV)

2.3. Observation 3

12-year-old SK boy, with no particular pathological history, who presented chronic headaches for 12 months. Two months before the neurosurgery consultation, the clinical picture was exacerbated with morning vomiting and a gradual decline in bilateral visual acuity resulting in bilateral blindness without seizures or sensitivomotor deficit. The entrance examination found a patient with a clear conscience (Glasgow score of 15/15), bilateral blindness, moderate intracranial hypertension syndrome and endocrine syndrome with hypothyroidism. A brain scan with injection of contrast product followed by magnetic resonance imaging (MRI) of the brain were carried out. They show an important expansive process in intra and supra sellar measured at 65 x 30.3 x 33.6 mm with a solidocystic component with calcifications suggestive of craniopharyngioma (figure 7, EF). Hormonal assay showed normal prolactinemia and hypothyroidism supplemented by oral levothyrox. Excision of the craniopharyngioma by craniotomy was performed with simple operative consequences. Anatomopathological examination of the operative specimen confirms an adamantine-type craniopharyngioma. A control postoperative brain scan found a large residue of the lesion of 47.7 x 30.1 x 34.5 mm (Figure 8). Adjuvant treatment with external radiotherapy using a three-dimensional conformational technique (RC3D) with multiple beams energy 6 to 10MV has been achieved. The dose of 54Gy in classic fractionation of 2Gy per session was used and dosimetric planning made it possible to obtain a treatment plan covering the target volumes according to ICRU 50 while respecting the dosimetric constraints on the organs at risk. The evolution was marked by a regression of clinical symptoms. At 15 months after radiotherapy, the patient presented no persistent symptoms apart from a decline in visual acuity rated at 2/10 on the left and 4/10 on the left.

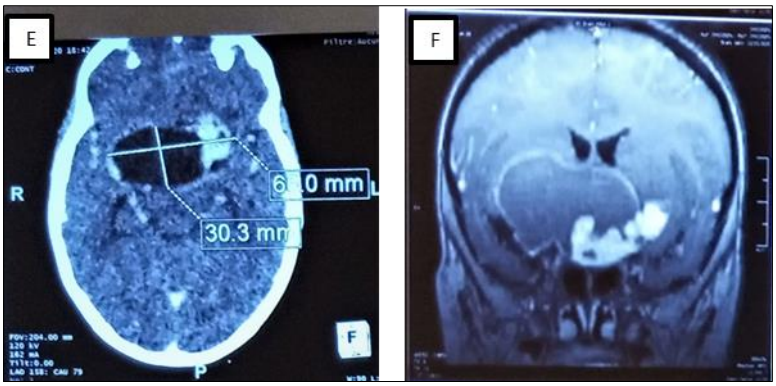

Figure 7 Expansive intra- and supra-sellar process measured with a solido-cystic component with calcifications suggestive of craniopharyngioma: E (CT image); F (MRI image)

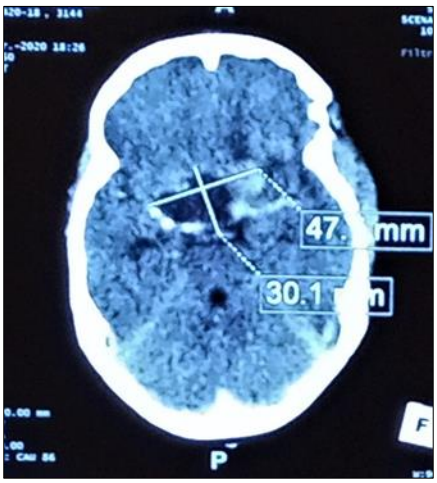

Figure 8 Post-operative control brain CT scan showing a large residue of the lesion

3. Discussion

We have reported three observations of craniopharyngiomas in infra- and supra-sellar children operated on and confirmed by pathological examination and having been treated with adjuvant external radiotherapy. It is a rare tumor since its incidence across the world is 0.5 to 2 new cases per million inhabitant representing 3 to 4% of intracranial tumors [1] and 1.3 new cases per million d 'living in the United States [4]. In children, they represent 10% of all intracranial tumors, and despite their embryonic origin they are exceptional before two years of age with a peak in frequency between 7 and 13 years. Childhood craniopharyngiomas are rare and histologically benign embryonic tumors with an incidence in France of approximately 20-25 cases per year, with a median age of 6 years [3]. Due to slow and variable growth with stopping phases; the symptoms appear in childhood or adolescence in 41% of cases, against 59% in adulthood. There is a slight male predominance (sex ratio: 1.3) [1] as confirmed by our three reported cases.

On the etiopathogenetic level, it has been considered since the work of Erdheim (1904) that craniopharyngiomas develop from epithelial remains of the Rathke pouch. This anatomical structure originates from an intracranial diverticulum of the stomodaeum, which originates from the anterior lobe of the pituitary gland. For the embryonic theory; craniopharyngiomas would come from these embryonic remains, located in the pars tuberalis and at the junction of this one with the anterior lobe of the pituitary gland. Other authors argue that craniopharyngiomas result from a metaplastic transformation of anterior pituitary cells (metaplastic theory) [1,5].

The nature of the tumor encountered in our patients is consistent with the adamantinomatous form, generally with a congenital onset, therefore the prerogative of children. This adamantine form is characterized by the existence of three components: cystic, fleshy and calcified. It is distinguished from that which develops in adults from the scaly part of the Rathke pouch, which is therefore papillary [6].

The clinical picture may associate, to varying degrees, endocrine disorders, ophthalmologic disorders, signs of intracranial hypertension (ICH) and related focal neurologic signs. The telltale signs are often amblyopia and signs of intracranial hypertension in children, growth retardation or delayed puberty in adolescents. The initial signs do not always attract the patient's attention. They can precede the diagnosis by several years, which is then made on the occasion of a worsening (loss of visual acuity, intracranial hypertension). In children, the call sign is visual in 30% of cases, but, upon diagnosis, the majority of patients actually have visual impairment. These visual disturbances may be related to compression of the optic pathways and / or be secondary to chronic HIC.

Signs of intracranial hypertension are very common in children and often revealing (60 to 70% of cases). Intracranial hypertension may be related to hydrocephalus through blockage of Monrö's holes or to the volume of the craniopharyngioma itself, especially in giant craniopharyngiomas, which often have cysts that can grow rapidly. Isolated headaches, without signs of intracranial hypertension, can be seen with distension of the dura mater of the sellar compartment in endosellar developing tumors.

Endocrine disorders can be linked to isolated damage to the pituitary gland and result in more or less complete panhypopituitarism. This is the case with endosellar starting craniopharyngiomas. But most often, and especially in suprasellar craniopharyngiomas, the endocrine deficit is secondary to an infundibulo-tubereal lesion disrupting the hypothalamic control of pituitary functions. Deficits are often associated, several lineages being affected in the same patient.The thyrocorticotropic axis is most affected during these deficits [1,3,7].

From a diagnostic point of view, even if the tomodensitometry in axial and frontal fine sections, associated if necessary with a sagittal reconstruction with injection of contrast product makes it possible to clearly identify the tumor; Magnetic resonance imaging (MRI) is the exam of choice for craniopharyngioma as it is for all midline pathology. The fleshy portion usually gives a hypointense on T1-weighted sequences and a hypersignal in T2. The cystic portion has a signal that is all the more intense on the T1 sequences as the cyst contains more cholesterin or methemoglobin. Calcifications are not visualized on MRI, but the absence of a localized signal makes it possible to guess them, even to draw their outlines [8,9].

From a therapeutic standpoint, the ideal management of this benign tumor should be complete surgical excision. All over the world and until the end of the 90s, neurosurgeons recommended a total excision of this histologically benign tumor, because it was assumed that its complete surgical excision should allow, in theory, to obtain a cure. However, the morbidity sometimes incompatible with a normal quality of life and the rate of recurrence despite the absence of an obvious residue [10,11] made people realize that in some cases complete excision could lead to unacceptable hypothalamic damage [12,13]. Therefore, the management of craniopharyngioma in children requires medical preparation by substitution treatment of the affected areas and by the appropriate use of multimodal treatment combining surgery and radiotherapy [14]. The transsphenoidal route is preferred in purely subdiaphragmatic craniopharyngiomas while supradaphragmatic must be approached endocranially [15]. This is a delicate surgery that can be limited by the invasion by the tumor of certain structures such as the side walls of the third ventricle, the optic pathways, the vascular structures and especially the hypothalamus. Performed by trained neurosurgeons, the procedure allows total excision in 60 to 70% of cases. In other cases, we will be satisfied either with simple decompressive surgery (partial excision: 10% of cases), or with subtotal excision leaving microscopic tumor residues in the invaded parenchyma (20 to 30% of cases), especially as adjuvant treatments are increasingly effective [1,12,16].

Since Kramer's work, many published series have demonstrated the effectiveness of radiotherapy [17,18]. Radiotherapy has no indication when tumor resection has been complete. In the event of incomplete removal of the tumor, some authors use it systematically to try to reduce or delay the risk of recurrence. It only seems to be indicated when there is proof of a radiological and / or clinical evolution of a tumor residue, especially if a reoperation seems too risky. In all these situations, it will be advisable to discuss in a multidisciplinary consultation meeting the indication of this radiotherapy by a benefit / risk balance, all the more so in children with a growing brain.

A distinction is made between conventional radiotherapy [19]: it is conventionally carried out with two to four fields centered on the lesion, with a division of five sessions per week, for five to seven weeks. The total dose delivered is a minimum of 50Gy and a maximum of 60 Gy. Currently, progress has been made by multiplying the beams which allows more precise dosimetry and better protection of risk areas. Our patients were treated by this conformational technique with 4 to 6 beams at a dose of 54Gy according to conventional fractionation. Endocardial radiotherapy [20] using beta-transmitters (P32, Y90, Au198, and Re186) implanted in the cysts. Its goal is the stabilization of cysts and not the treatment of the fleshy tumor and finally stereotaxic radiotherapy [21] or radio surgery; reserved for small tumors or residues less than 2 cm, is currently expanding. This technique is performed either using a gamma knife or with a linear accelerator. The spatial delineation of the tumor is specified in stereotaxic condition. Because of the risk of

radionecrosis in children and in this type of pathology, proton therapy thanks to its Bragg peak appears to be the radiotherapy technique of choice, best sparing the functional tissues in the surrounding area [22]. In some teams, the presence of a cystic component of the craniopharyngioma is like a "contraindication" to radiotherapy, according to them the cyst initially responds poorly to the rays and could initially progress, sometimes rapidly [23]. Intracavitary chemotherapy with bleomycin and by injection of alpha interferon thanks to its affinity for epithelial tumors, is indicated in cystic craniopharyngiomas [24] even if this bleomycin-based treatment is criticized for its major complications (pulmonary fibrosis). .

In radical surgery, the risk of recurrence depends on the quality of the resection [16,25]: 15% for the resections considered as total, 35% for the subtotal resections, 70% for the partial resections. In the event of incomplete resection, radiotherapy reduces this risk to a rate close to that observed after total resection, at the cost of its own complications. Given the difficulty of reoperations, the treatment of progressive recurrences generally calls for radiotherapy, if this has not already been performed. With prolonged and close follow-up, most recurrences should be discoverable at a small volume, making conformational irradiation, proton therapy or radiosurgery possible, and not requiring further decompression intervention. This treatment makes it possible to hope for a definitive cure in 70 to 80% of cases. There will remain, however, a group of patients who will escape treatment, ultimately with an unfavorable outcome [1].

In our observations, despite the relatively low mean follow-up, we noted very significant objective responses with this multimodal approach to partial surgery associated with conventional radiotherapy.

4. Conclusion

Craniopharyngioma is a rare benign tumor in children. Due to a long latency, the diagnosis is often late with intracranial, endocrine and especially visual symptoms. The management is multidisciplinary and must be discussed on a case-by-case basis in a multidisciplinary consultation meeting. The current trend in the era of modern radiotherapy is dominated by partial surgeries followed by adjuvant treatments allowing functional prognosis to be maintained with acceptable results in terms of locoregional tumor control.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

The authors declare no conflict of interest.

Statement of Ethical approval

The consent of legal guardians and their approval was obtained for the publication of these cases.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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