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Clinical Paper
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Management of nasopharyngeal teratomas associated with cleft palate

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Abstract. Nasopharyngeal teratomas are rare tumours, responsible for a high birth mortality rate from acute respiratory distress. Palatine localization can lead to an embryopathogenic mechanical obstacle responsible for a cleft palate. The aim of this study was to update current knowledge concerning the management of this rare pathological association.

We conducted a multicentre, retrospective study by case analysis. The inclusion criteria were patients of any age under care for a nasopharyngeal teratoma associated with a velopalatine cleft. The diagnosis of the teratoma was confirmed by histological analysis.

Seven cases were included in the study: three cases from the University Hospital of Lille, one from the University Hospital of Caen, one from of the University Hospital of Toulouse, and two from of the University Hospital of Amiens. Approximately 30% of patients experienced acute respiratory distress at birth, necessitating oro- or nasotracheal intubation. The surgical excision was performed in the first 5 months of life for all patients and in a single operative time for 70%. There was no recurrence.

Therapeutic management of nasopharyngeal teratomas associated with cleft palate at birth is multidisciplinary and is based on surgical excision. In the absence of other associated pathologies, the prognosis is favourable.

Key words: prenatal diagnosis; teratomas; respiratory distress at birth; velopalatin cleft.

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Teratomas are complex tumours composed of tissues from the three embryonic layers foreign to the region that shelters it. Teratomas are found at birth in one of 4000 cases, representing 25–35% of neonatal tumours[1]. They occur most frequently in the sacrococcygeal region (45% of teratomas)[2]. Cervicofacial teratomas represent 5–15% of cases[3].

The term 'epignathic tumuors' should be reserved for tumours originating from the jaw[4]. These lesions can extend to the sphenoidal, endobuccal and pharyngeal regions. According to Levine et al.[5], the incidence of oropharyngeal teratomas is between 1 in 35,000 and 1 in 200,000 live births, approximately 2–3% of all teratomas. They occur mostly in females, with a 3:1 ratio[6].

The appearance of nasopharyngeal teratomas varies according to the size, degree of tissue heterogeneity, and degree of tissue maturation[7]. These lesions may be defined as mature, immature, or mixed, depending on tissue maturity and the stage

of embryonic development[8]. Most nasopharyngeal teratomas are benign, but rare cases of malignant and metastatic lesions have been reported[9].

Malformations are associated with such teratomas in 6% of cases[10] (bifurcation of the tongue, meningoencephalocele, pituitary duplication, etc.). Cleft palate is the most common associated abnormality. This type of cleft palate is of mechanical origin, the teratoma being an obstacle for the fusion of the hard palate[11]. Neither a genetic association, nor exogenous factors, such as carcinogenic drugs, have been demonstrated to be associated with their occurrence.

The predominant physiopathological hypothesis is the implantation of totipotent cells from the Rathke pouch[12], which become trapped in the nasopharynx and undergo disorganized developement after escaping normal control mediated by growth factors.

The most recent classification was reported by Wittstock et al.[13], which describes three types: (1) dermoid (most frequent) tumours, composed of one or two germ layer(s) (ectoderm and/or mesoderm); (2) teratoid tumours, composed of all three germ layers, but which are poorly differentiated; and (3) the true teratomas, composed of well-differentiated tissues derived from all three germ layers. The epignathus or 'fetus in fetus' is included and classified as a true teratoma because it contains all three germ layers in a well-differentiated form (recognizable organs or limbs). This is currently the most-used classification and it was used in this study.

Antenatal ultrasound between the second and third trimesters can show the presence of an oral or pharyngeal mass in 20–50% of cases[14]. The velopalatale cleft is rarely seen because the teratoma is interposed in the space between the two palatal shelves. Three-dimensional (3D) ultrasound or magnetic resonance imaging (MRI) are proposed if there is strong suspicion[15].

At birth, neonatal care is multidisciplinary, initially provided by paediatric reanimation specialists and then surgeons to limit the occurrence of serious complications. Indeed, there is a risk of acute obstructive respiratory distress in 35–45% of cases[16], with mortality rates sometimes reaching 100%[17]. Appropriate imaging (computed tomography (CT) scan and MRI) is essential for locoregional exploration and planning care.

Very few cases are described in the literature and the management is not standardized. The aim of this study was to update current knowledge concerning this pathological association, to study the treatment proposed in the four departments concerned, and to compare it with the findings found in the literature.

Materials and methods

This was a retrospective multicentre analysis of medical records from the Departments of Maxillofacial Surgery of the University Hospital of Caen, Paediatric Surgery of the University Hospital of Toulouse, Maxillofacial Surgery of the University Hospital of Amiens and Plastic Surgery of the University Hospital of Lille.

The inclusion criteria were patients of any age under care for a nasopharyngeal teratoma associated with a cleft palate. The diagnosis of the teratoma was confirmed by histological analysis. We excluded patients with a nasopharyngeal teratoma not associated with a cleft palate, those with a histological analysis of a tumour other than a teratoma, and those who were stillborn.

Communication with the surgeons and specialists responsible for the patients, and consultation of the medical records allowed us to study the time course of surgical management, the clinical and paraclinical evaluation carried out, management of the cleft, and monitoring and evolution of the patients. We compared the antenatal and neonatal care between these four centres with that reported in the literature.

Results

Seven patients, treated between 1991 and 2015, were included in the study. There were three cases from the University Hospital of Lille, one from the University Hospital of Caen, one from the University Hospital of Toulouse and two from the University Hospital of Amiens. Most of the patients were female, with 70% girls (five of seven patients).

The average age of birth for all patients was 38 weeks of amenorrhea. Births were equally divided between natural and caesarean delivery (no data for one case). The average weight at birth was 2750g (from 2500 to 3820 g, normal range at 3500 g), the mean length was 48 cm (from 43 to 52 cm, normal range at 50 cm), and the average cranial circumference was 34 cm (from 32 to 36 cm, normal range at 35 cm). Parents had no history of teratoma and the average age of the mothers was 28 years.

Antenatal assessment (Table 1) allowed the diagnosis in a single patient (14%), case 7 (Fig. 1), for which the ultrasound at 28 weeks of amenorrhea detected an intraoral tumour, confirmed by 3D ultrasound and foetal MRI. This was the only patient treated at birth using an artificial ventilation technique, such as the ex utero intrapartum treatment (EXIT) procedure.

Among the other patients, two (28%) experienced acute respiratory distress at birth (Table 1), requiring orotracheal intubation (cases 3 and 6). Dyspnea was evident in the patient of case 1 only when taking a bottle for feeding. Complete assessment of the lesion by exploration under general anaesthesia, combined with biopsies, was performed for three patients (cases 3, 4 and 5). Clinically, the palpated intraoral mass was homogeneous or heterogeneous, soft, and well delimited. The mass extended to the nasal cavity in all cases (Fig. 2). Two patients (cases 5 and 3) had a second simultaneous teratoma. Case 5 presented a second teratoma within the buccal floor, causing lingua bifida. For case 3, the second teratoma was found at the anterior part of the palate, causing a cleft lip.

A CT scan and MRI were performed in the seven patients to localize the tumour, to characterize it, to search for associated pathologies, and to confirm the cleft palate. A well-delimited, pediculated, heterogeneous tumour, appended to the vomer bone and/or the sphenoid was found in all cases (Fig. 3). No endocranial extension was discovered.

Tumour markers, Alpha-fetoprotein (AFP) and Beta-HCG (βHCG) were assayed in four patients (cases 4, 5, 6 and 7) as part of the diagnosis. AFP levels were elevated only for cases 6 and 7. AFP levels rapidly decreased after surgical resection, before returning to normal. The AFP assay was used in case 7 for secondary monitoring. The levels of βHCG were normal for all cases.

Associated lesions (Table 1) were found in three of our patients, in addition to the teratomas and cleft palate. Case 1 showed a duplication of the pituitary gland (Fig. 4) with a hamartoma of the third ventricle, associated with Klippel–Feil syndrome (short neck and partial fusion of the cervical vertebrae) and Pierre Robin syndrome. Case 3 showed a cleft lip and a meningocele located opposite the teratoma (Fig. 5), diagnosed by imaging and confirmed during teratoma excision by visualization of encephaloid tissue and the flow of cerebrospinal fluid. Case 5 showed a lingua bifida of mechanical origin, associated

Table 1. Clinical characteristics and management of the seven patients.

	Histology	Prenatal diagnosis	Neonatal complications	Associated lesions	Surgical excision of the teratoma	Closing of the Velopalatine	Surveillance period
Case 1 (Lille)	True mature teratoma	No	No	- Duplication of the pituitary gland with a hamartoma of the third ventricle - Pierre Robin syndrome - Klippel Feil syndrome	1 month (1 time)	1 time at 11 months	22 years
Case 2 (Lille)	True mature teratoma	No	No	No	5 months (1 time)	1 time at 18 months	15 years
Case 3 (Lille)	True mature teratoma	No	Acute respiratory distress => orotracheal intubation	- Lip cleft - Sphenoidal Meningoencephalocele	2 days (1 time)	1 time at 16 months	26 years
Case 4 (Caen)	Mature dermoid teratoma	No	No	No	5 months (1 time)	2 times: Soft palate at 8 months Hard palate at 17 months	4 years
Case 5 (Toulouse)	2 immature dermoid teratomas (vomer bone and hard palate)	No	Non	- Bifid tongue - Duplication of the pituitary gland with a hamartoma of the third ventricle	10 days and 20 months (2 times)	Soft palate at 20 months Hard palate not closed	2 years
Case 6 (Amiens)	True mature teratoma	ND	Acute respiratory distress => orotracheal intubation	No	13 days (one time)	ND	ND
Case 7 (Amiens)	2 True matures teratomas (hard palate)	Yes => (EXIT Procedure)	No	No	J0 (EXIT Procedure) et 7 months (2 times)	2 times: soft palate at 7 months hard palate at 21 months	8 years
Average		14%	28%		Between 1 and 2 months 1 time in 70% of cases		13 years

with a duplication of the pituitary gland and a hamartoma of the third ventricle.

Surgical excision was performed for 70% of our patients in a single surgery. Two patients (cases 5 and 7) underwent a second excision to resect residual tumour tissue. Surgical excision was performed in all our patients by an intraoral approach. Cervicotomy was also required in one patient because the teratoma had a parapharyngeal extension. None of our patients presented complications. The teratomas were delineated and cleaved well surgically. The dissection was nevertheless careful so as not to damage adjacent structures. There was no recurrence after surgery and complete excision, for any of our patients after a mean follow-up of 13 years (range 2–26 years).

Histologically (Table 1), five patients had a true teratoma, according to the Wittstock classification[13]. The other two cases were dermoid-tumour-type teratomas. All patients had mature teratomas, apart from case 5 with an immature teratoma. No criteria of malignancy were found.

The management of the cleft (Table 1) followed the standard protocol at each hospital for cleft-palate repair, according to the timing of the subsequent surgery. Only one patient (case 5) did not undergo complete velopalate closure to allow surveillance. A palatal obturator was placed instead. Follow-up for our patients was strictly clinical. However, patient 7 was more regularly tested with the AFP assay, and an MRI was performed to ensure the absence of recurrence.

Discussion

In our series, prenatal assessment allowed the diagnosis a nasopharyngeal teratoma in a single patient (case 7), during the second trimester (14%), which is lower than the rate found in the literature (20–50% of diagnoses made during the second trimester[14]). This can be explained by the presence of two cases in our study that were more than 20 years old. Ultrasound techniques have improved since then. In addition, data, including antenatal diagnosis, are missing for case 6.

In the case of prenatal diagnosis, the mode of delivery depends on the location of the lesion, its size, the degree of tracheal obstruction, the degree of polyhydramnios, and gestational age. Diagnosis before birth also has the advantage of allowing psychological preparation for the parents.

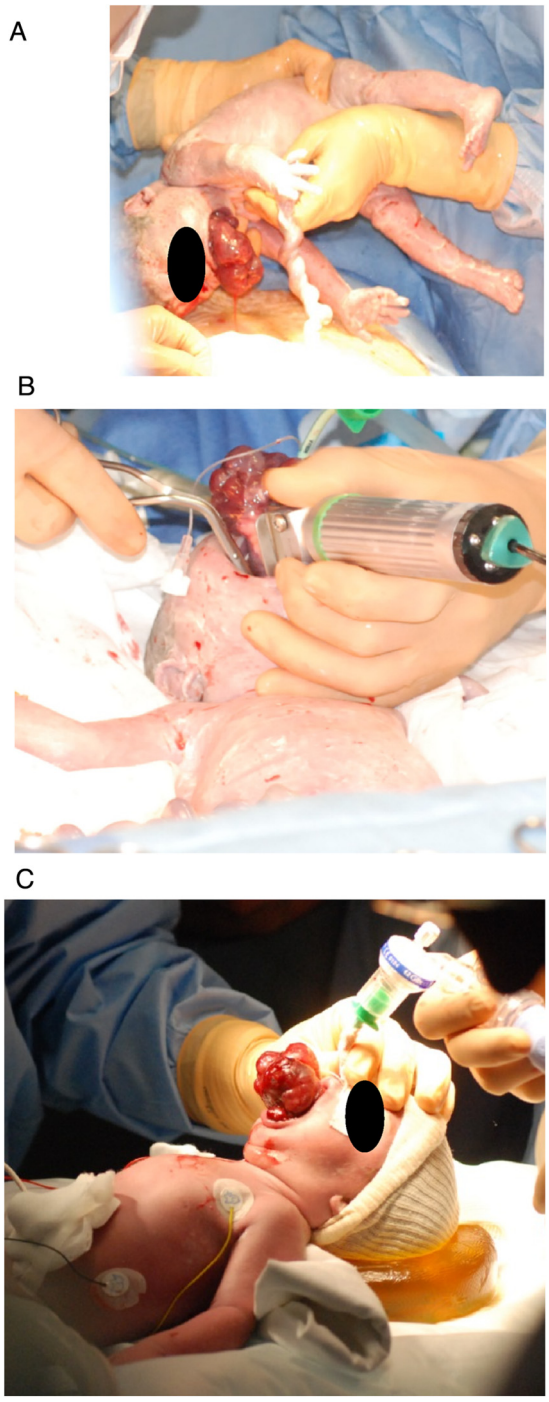

Fig. 1. Case 7: EXIT (ex utero intrapartum treatment) procedure with nasotracheal intubation and the tumour surgery (courtesy of Prof. Devauchelle, Universitary Hospital of Amiens, France). (A) Caesarean section; (B) nasotracheal intubation before sectioning of the umbilical cord; (C) profile view of the teratoma after the excision.

Case 7 in which the tumour was diagnosed antenatally, presented a strong suspicion of upper-airway obstruction. It was therefore decided to use an artificial ventilation of the EXIT procedure type and perform surgery before clamping the umbilical cord. A caesarean approach was performed with extraction of the newborn without clamping of the umbilical cord. Nasotracheal intubation was performed under fibroscopy and perfusion maintained by the umbilical route. At the same time, removal of the obstructive tumour was performed. The umbilical cord was then clamped and severed.

There are two techniques currently used in cases of strong suspicion of upper-airway obstruction in neonatals[18]: the ex utero intrapartum treatment procedure and the operation on placenta support (OOPS) technique.

If there is suspicion of airway obstruction following prenatal diagnosis, the presence of a maxillofacial surgeon or an otorhinolaryngologist in the delivery room is recommended, even if there is no detectable compression of the upper airways. In the absence of a diagnosis prior to birth, possible respiratory distress is managed by anaesthetists, and if possible, neonatal reanimation specialists and paediatricians. Changing the position of the newborn and traction on the tumour may provide temporary improvement. Oropharyngeal intubation (or, if possible, immediate nasotracheal intubation to allow surgery of the teratoma) and, if necessary, tracheotomy are often required.

In addition to patient 7, who required the EXIT procedure, two other patients in our series (approximately 30%) experienced acute respiratory distress at birth, requiring orotracheal intubation (cases 3 and 6). Dyspnea occurred in the patient of case 1 when taking the bottles for feeding, but without the need for intubation or tracheotomy. These disorders were resolved after surgery.

All patients underwent clinical and paraclinical assessment (generally under general anaesthesia) to locate the teratoma, determine the size, search for other associated lesions, perform biopsies and develop the therapeutic approach for excision. Care must be multidisciplinary.

Tumour markers levels were performed for four of our patients and were positive (increase in AFP) for two (50%), showing the presence of mature benign teratomas.

There was no data for cases 1, 2 or 3. In the study by Billmire et al.[19], preoperative AFP levels were elevated in 20% of patients with teratomas and returned to normal after surgical excision. Elevated levels of these hormones have a positive predictive value. The absence of elevation, however, does not eliminate the diagnosis. This assay is therefore useful for preoperative diagnosis and patient follow-up to monitor the possibility of incomplete excision or local recurrence, if the preoperative level is increased

The treatment of teratomas is surgical. In the early 2000s, mortality due to nasopharyngeal teratomas was 80–100% in the absence of surgical treatment in several series[20]. All patients who died did so from

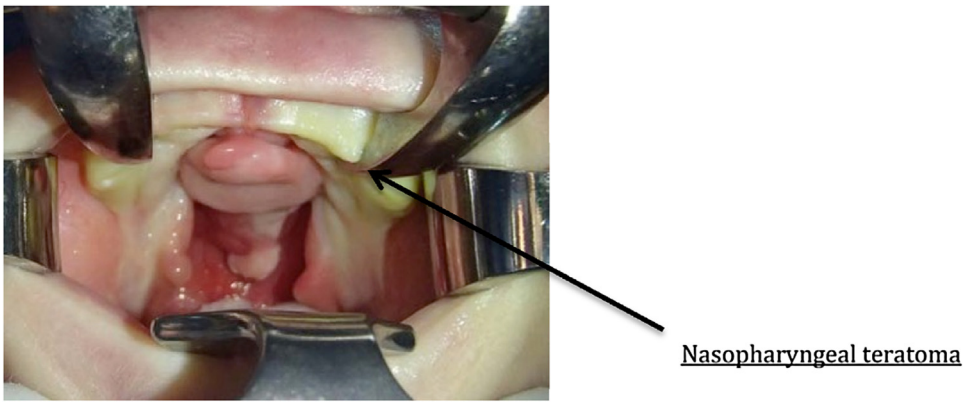

Fig. 2. Teratoma appended to the nasal septum (case 4).

respiratory distress due to obstructive syndrome, causing cerebral anoxia. Those who survived had severe neurological sequelae related to cerebral anoxia (e.g., tetraplegia). Thus, surgery should not be delayed for a long time. It is advisable to remove the tumour, even if it does not appear to be an obstacle or life-threatening, because of its potential for rapid growth and resulting impediment to the development of neighbouring healthy structures.

In our series, surgical excision was rapidly performed in the three patients with acute obstructive respiratory distress (D0, D2 and D13). In the absence of acute respiratory distress, the teams opted for excision of the teratoma, without urgency, during the first 6 months of life. There were no postoperative complications. Reported postoperative mortality in the literature is low[21,22]. The resection must be complete because of the risk of previously described malignant degeneration[23]. Additional surgeries are possible in cases of incomplete excision to avoid recurrence[24]. Two patients (cases 5 and 7) had surgical excision in two stages due to an incomplete excision. The survival rate of our cases following resection was 100%, with a follow-up of more than 20 years for cases 1 and 2. There was no local recurrence after a complete resection.

A dozen cases of palatal teratomas have been reported in the literature since 2000. All patients survived following surgery with no signs of recurrence. According to Wong et al.[25], patients with a benign nasopharyngeal teratoma have an excellent prognosis following complete resection, with a survival close to 100%.

Management of the cleft should be secondary to surgical excision of the teratoma, to ensure its removal while still benign, and performed by a multidisciplinary team as for other patients with clefts. Timing of the operation and the surgical technique depend on the standard practices of the surgical teams. After complete excision of the teratomas without recurrence of teratomas, these patients are simply considered as those with conventional clefts. Based on their age, they receive maxillofacial surgeon, otorhinolaryngologic, orthophonic and orthodontic follow-up.

The surgical technique used for cleft palate closure of all our patients was the same as that normally used in each department. The timing respected the normal schedule of each team, except for a shift in one department due to the time of excision of the teratoma. The normal schedule for the management of the velopalatine cleft is not generally specified in the literature. It is therefore difficult to compare our cases with those in the literature to determine whether there are dif-

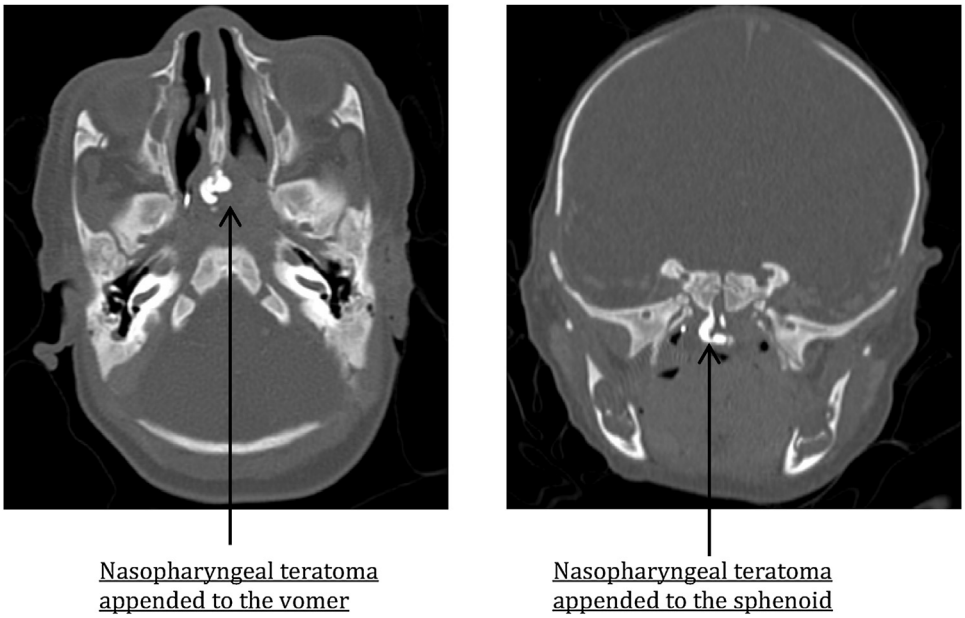

Fig. 3. Computed tomography scan of nasopharyngeal teratoma appended to the vomer bone and the sphenoid (case 4).

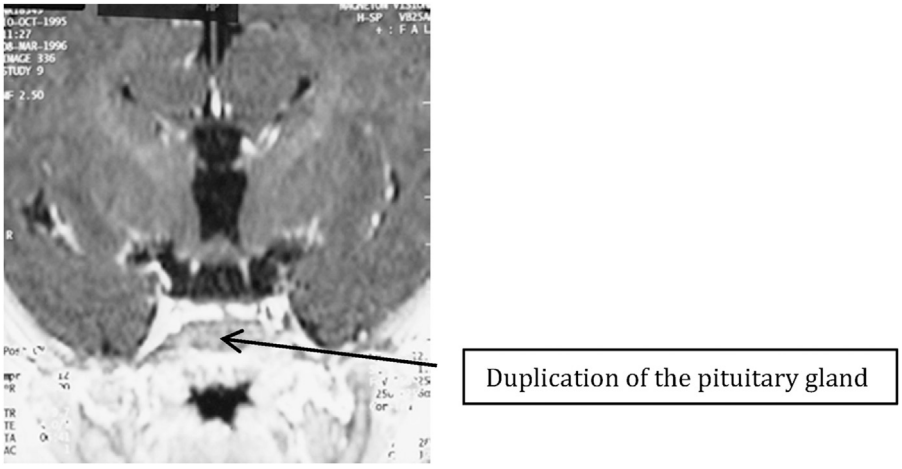

Fig. 4. Magnetic resonance imaging T1 showing duplication of the pituitary gland (case 1).

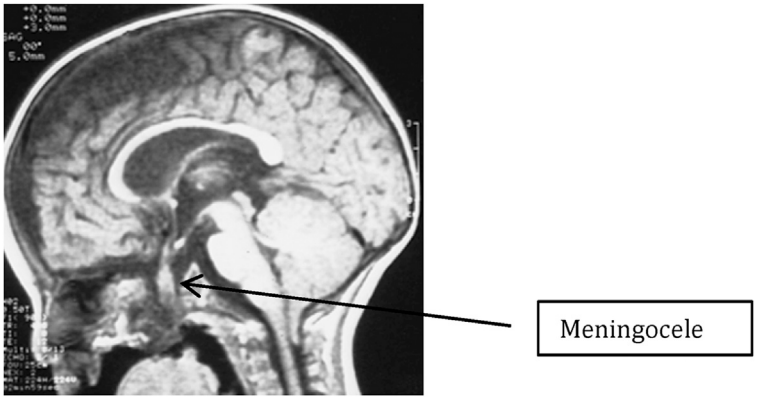

Fig. 5. Patient with a meningocele (case 1).

ferences in terms of type and duration of care.

Follow-up is primarily clinical. All patients have entered a standard assessment for their cleft with appropriate multidisciplinary management. However, imaging associated with tumour marker assays can be performed in cases of suspected incomplete excision or clinical suspicion of local recurrence.

In conclusion, nasopharyngeal teratoma associated with a cleft palate is a rare entity.

Management requires early excision of the teratoma. Management of the cleft should be based on the usual schedule of departments and after complete excision of the teratoma.

Follow-up of the teratoma is performed as part of the multidisciplinary follow-up of the cleft.

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Competing interests

The authors declare that they have no conflicts of interest.

Ethical approval

In France, retrospective studies do not fall under the opinion of an ethics committee (law Jardé of 5 March 2012).

Patient consent

Not required.

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