and trauma.[4] Vascular malformations do not tend to exhibit a proliferative stage followed by stabilization and involution as seen in hemangiomas.[5] In the absence of a life-threatening indication, management is planned through multidisciplinary teams and can be handled with a single operation or a staged fashion. Treatment centers around sclerotherapy, with or without embolization and complete surgical excision. Subtotal resection may be required due to invasive growth into unresectable structures or as a bail-out procedure for patient stabilization in an emergency. It should be noted that subtotal resection carries increased risks of severe hemorrhage and is not a definitive procedure with high risk of recurrence. In rare cases, this may be life-threatening, particularly in the case of airway bleeding or relative blood loss seen in neonates and infants. Airway complications cannot be underestimated. Even with nonoperative sclerotherapy, inflammation and swelling resulting in airway loss can result.[6]

Vessel sealing instruments are commonly used in other fields of surgery for ligamentous dissection as well as efficacious division of vascular tissue such as thyroid, omentum, and mesentery. They have also been described in vascular control of head and neck tumors, including thyroid surgery and intra-oral cancer surgery. In a single-center case-control study, Kanno et al determined that vessel sealing devices in head and neck tumor resections, ''significantly reduced intraoperative blood loss [with] no differences between the 2 groups with regard to postoperative complications and recurrence.''[7]

There is a paucity of published literature of large VMs being managed with energy devices. Hosny et al performed a single-center study of 14 patients with VMs of the head, neck, trunk, and extremity. Two major complications were seen in their review including stroke/TIA and 1 death, demonstrating the occasional severity of these lesions. The complications were not felt to be related to the energy devices, in fact, the authors stated that these devices will improve the safety and broaden the role of surgical management of large VMs.[8] We agree with the authors' comments that vascular clamps and suture ligation of vessels can be difficult and tedious, and traditionally, VMs are resected with laborious suture ligation which can put both blood vessels and lymphatic channels at risk of tearing during dissection for proximal and distal vascular control. Vessel sealing devices have the advantage of gaining hemostasis during dissection of vessels 8 mm and larger,[9] and reliably seal surrounding lymphatic channels that may be at risk during traditional dissection/suture ligation techniques.[10] Common vessel sealers on the market are the Impact Ligasure Exact by Medtronic, Enseal, and Harmonic Scalpel by Johnson and Johnson, Bowa Lotus torsional ultrasonic scalpel from Bowa Electronic, and Thunderbeat from Olympus, among others. In the cases discussed above, surgical technique included extensive use of vessel sealing devices. Similarly, Hosny et al state that ''All the conventional techniques and instruments like monopolar/bipolar diathermy, sutures, [and] vascular clamps were successfully replaced by the vessel sealing devices.''

Similar to the published literature, our patients went on to receive additional procedures following primary resection for control of tributary vessels and recurrence. Recurrence rates may be higher when removing lesions in pediatric patients for acute indications. A definitive rate of recurrence is difficult to cite as published series are small, size and flow may affect recurrence rates, and large VMs followed with imaging may show radiographic recurrence that is not bothersome to the patient and may not go on to receive intervention. The effect of different surgical techniques, particularly use of vessel sealing devices, on rates of recurrence requires further study.

CONCLUSION

Each of the above patients had a large lesion that achieved successful surgical resection with minimal morbidity following a swift operation. Massive VMs, particularly of the head and neck, are complex lesions that are likely treated best at tertiary care facilities offering multidisciplinary interventions with care teams familiar with treatment options. Surgical excision, whether emergent or staged, can be complex and itself involves the risk of life-threatening bleeding. The use of vessel sealing devices may improve the safety and efficiency of an otherwise difficult dissection and provide rapid hemostasis in both children and adult patients. Subsequent minor revisions and repeat sclerotherapy may be expected and patients and families should be prepared for possible reintervention.

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Adult Saethre-Chotzen Syndrome: A Unique Abnormal Breathing Pattern

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Abstract: A 35-year-old male with Saethre-Chotzen syndrome presented with severe complaints. Neuroimaging showed a Chiari-I malformation, mild ventriculomegaly, a syrinx of the wide central canal, and various cerebral vascular anomalies including a large occipital emissary vein on the right. Ultrasound of this vein confirmed

blocking of the outflow-track when turning his head to the right, which also provoked the headaches and bruit. Polysomnography revealed severe positional sleep apnea with a mixed breathing pattern, the central components consisted of periodic breathing with, at times, crescendo-decrescendo reminiscent of a Cheyne-Stokes versus Biot breathing pattern, pointing to possible brain stem/pontine problems. Continuous positive airway pressure was initiated, and the patient was instructed to avoid sleeping in the right lateral position. One year later, nearly all his complaints have resolved. A questionnaire was sent to all adult Saethre-Chotzen patients in our craniofacial unit, none reported any of the severe symptoms as described by our index case.

Key Words: Central sleep apnea, Cheyne-Stokes breathing, craniosynostosis, obstructive sleep apnea, sleep disordered breathing, venous hypertension

Saethre-Chotzen syndrome is associated with sleep-related disordered breathing (SRDB) and intracranial hypertension (ICH).[1] Here, we describe a 35-year-old male with Saethre-Chotzen syndrome, who presented with severe neurological symptoms and an unusual cause of SRDB.

Clinical Presentation

A 35-year-old male with Saethre-Chotzen syndrome (*TWIST1 c.165ins10*) presented to our clinic after neurology referral because of unexplained headaches. He was born with bicoronal synostosis and had previously undergone 3 cranial vault expansions (all fronto-supraorbital advancement) when aged 3 months, 16 months, and 13 years as treatment of recurring, severe supraorbital retrusion. Papilledema was never diagnosed. Two years before this referral, he had been admitted to a neurology ward because of thunderclap headache with loss of consciousness. At that time, he had had headaches and tingling of the hands and feet for some while. There was no tongue biting or incontinence associated with his loss of consciousness, and a brain computed tomography (CT) scan was normal. Since then, other complaints arose, including:

1) continuous headaches and sense of pressure near the occiput, worsening in attacks, mainly when bending over, sneezing or coughing;
2) photophobia and daily blurred vision with eye floaters when getting-up in the morning, lasting 10 minutes;
3) hearing a bruit in the head;
4) daily hemiparesthesia of the right upper and lower limbs in sitting position – independent of any headache or eye problems – lasting 30 seconds, and stopping with movement.

Neurological examination revealed uncrossed diplopia when gazing to the left. Cerebral magnetic resonance imaging (MRI) showed cerebellar tonsillar herniation (TH) of 6 mm (ie, Chiari-I malformation) and mild ventriculomegaly. In our outpatient clinic, we found out that when he worked more than 2 hours he would often have worsening headaches, and collapse. Also, the bruit worsened when turning the head to the right and he snored significantly during sleep, waking-up tired. On examination, he did not have nasal septum deviation, or midface or mandibular hypoplasia. Fundoscopy and optical coherence tomography showed no papilledema or atrophy of the optic nerve head. Cranial CT angiography showed a persistent falcine sinus, with an aberrant venous outflow track, a missing transverse sinus on the left and a large occipital emissary vein on the right side (Fig. 1). Cerebral MRI showed stable ventriculomegaly, the Chiari-I malformation and a small syrinx of the wide central canal. An ultrasound scan of the occipital emissary vein confirmed blocking of the venous outflow track when turning the head to the right, which provoked the headaches and the bruit. Polysomnography (PSG) revealed positional sleep apnea with an apnea hypopnea index (AHI) of 37.5/h (AHI $\geq$30/h is considered "severe"),[2] which worsened to 85.5/h in the supine position. The pulse oximetry measured oxygen-hemoglobin (SpO_2) desaturation index (ODI) was 44.5 times/h ($\geq$ 30 episodes/h with fall in $SpO_2 > 3\%$ considered severe).[2] The arousal index was 27.5 awakenings/h. A mixed breathing pattern with central and obstructive components was diagnosed, the central components consisted of periodic breathing with, at times,

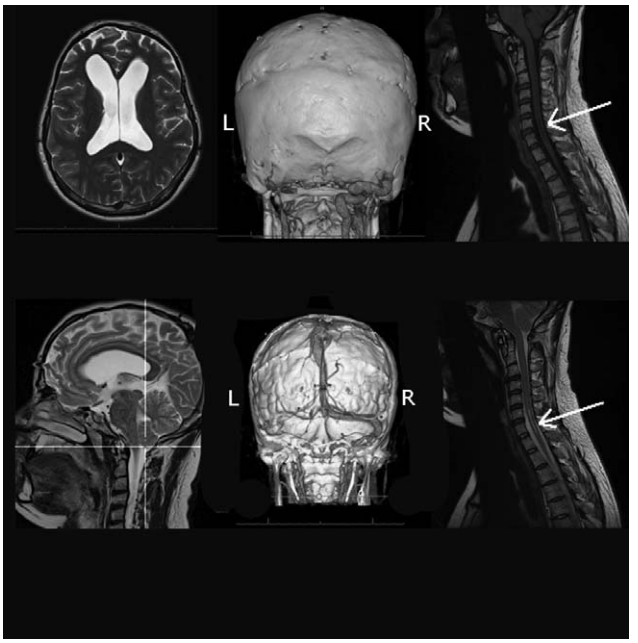

FIGURE 1. Neuroimaging. Upper, left: mild ventriculomegaly. Lower, left: 6 mm Chiari-I malformation. Upper, middle: large occipital emissary vein at the right. Lower, middle: missing left transverse sinus. Upper and lower, right: small syrinx of the wide central canal.

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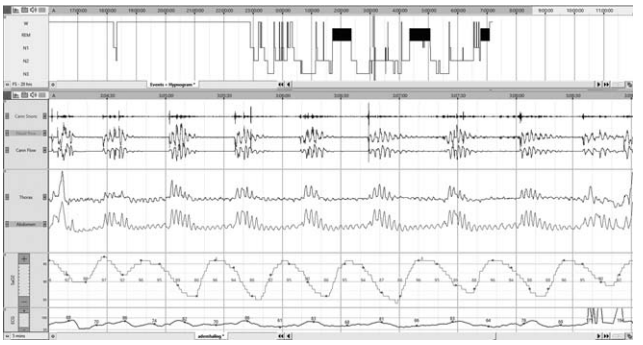

FIGURE 2. Polysomnography with sleep staged diagram showing Cheyne-stokes versus Biot like breathing. W – awake.

crescendo-decrescendo reminiscent of a Cheyne-Stokes breathing (CSB) versus Biot pattern (Fig. 2). To exclude airway obstruction at the base of the tongue, the PSG was repeated while using a tailor-made mandibular reposition device (MRD). Since the results of this PSG were identical to the initial study without the MRD, the sleep apnea was treated with night-time continuous positive airway pressure (CPAP) support. Additional tests were performed to exclude underlying congestive heart failure, neurological disease or renal disease causing CSB,[2] and were within normal limits. A year after starting night-time CPAP, the patient feels much better, and nearly all of his complaints have resolved, including the early morning headaches, the ophthalmological complaints, hemiparesthesia, and tiredness.

Family members: The patient described above has a 33-year-old brother, who visited the outpatient clinic with his 9 months old daughter, both have a *TWIST1* mutation *(c.152_161dup10)*. The 33-year-old unoperated brother had complaints of snoring and tiredness during daytime, with no palpable vessels in the head/neck region. PSG showed mild OSA, with an AHI of 12.5 and an ODI of 18, which was treated with expectant management. CT angiography and MRI studies showed no abnormalities. The daughter had synostosis of the coronal sutures and the sagittal suture partially. She underwent occipital expansion at the age of 9 months, and never had papilledema on repeated fundoscopies during follow-up. Her skull growth was normal postoperatively, she had no complaints during sleep, and MRI studies did not show abnormalities.

Questionnaires

Pediatric and adult patients with Saethre-Chotzen syndrome visit our outpatient clinic. In order to assess neurologic complaints in our adult patients with Saethre-Chotzen syndrome, we sent a questionnaire to all patients with Saethre-Chotzen syndrome who were aged > 18 years and to parents who had tested positive for genetic mutations. In total, 15 of 26 patients returned the questionnaire. The median age of the participants was 41 years (interquartile range 29.4–51.8). None reported any of the severe symptoms described by our index case.

DISCUSSION

In this case, severe positional sleep apnea with obstructive and central components was diagnosed, with the central components showing periodic breathing with, at times, a crescendo-decrescendo pattern, reminiscent of a CSB breathing pattern versus Biot breathing. However, neurological, renal and cardiovascular comorbidities were excluded. To date, we had not seen this unique breathing pattern in our craniosynostosis clinic Saethre-Chotzen syndrome population. Moreover, none of our other Saethre-Chotzen syndrome adults responding to a questionnaire reported any of the severe complaints experienced by the index case. There are several factors that could influence the unique breathing pattern in this patient, which include, ventriculomegaly, a Chiari-I malformation, a significant syrinx and the large occipital emissary vein.[3,4] We postulate that the combination of these abnormalities, could lead to any of the following conditions: an altered sensitivity to partial pressure of carbon dioxide (pCO_2), that is, increased because of cortical or forebrain pathology or decreased because of brain stem disease/ compression/ pressure); an increased pCO_2 control of the breathing threshold from brain stem abnormalities, a loss of cerebral blood flow response to changes in pCO_2; or, an abnormal vascular blood flow transit time because of abnormal venous return.[5–7] Given the fact that the complaints resolved after initiating CPAP, it is likely that the pCO_2 control normalized during sleep.[6] Moreover, as the patient likely suffered from postural obstruction of the occipital emissary vein, the patient was instructed to avoid sleeping on the (lateral) side of the collateral, which could have improved venous return. Anatomical variations or abnormalities in the venous compartment of the head and neck are common in Saethre-Chotzen syndrome, and are correlated to the presence of papilledema.[8,9] Given the venous compartment abnormalities in our patient, it seems likely that the venous outflow is compromised and that the emissary vein functions as a bypass for the intracranial blood flow.[8] The bypass might be compressed in the supine position, which further decreases the cerebral venous outflow, and thereby further enhances the increased cerebral blood flow associated with OSA.[6] The finding that the headaches in this patient worsened and that the flow in the emissary vein stopped when turning the head to the right, affirms this hypothesis. It is therefore likely that our patient developed ICH when turning the head to the right for a prolonged amount of time. In conclusion, we report and highlight this case because we are concerned that there may be other similarly at-risk patients in the Saethre-Chotzen syndrome population that craniofacial centers should be aware of. Moreover, we recommend performing a sleep study and a cranial CT angiography/MR-scan in adult Saethre-Chotzen patients who present with severe complaints.

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