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Original Article

Unpredicted respiratory arrest following hypoglossal nerve palsy during subarachnoid hemorrhage: Experimental study

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Abstract

Aim: Although acute respiratory arrest is the most dangerous complication of subarachnoid hemorrhage; if there is any association between hypoglossal nerve-tongue palsy induced acute mechanical upper airway obstruction has not been extensively described so far. Our aim is to evaluate if there is a relationship between hypoglossal ischemia-tongue paralysis and upper airway obstruction during subarachnoid hemorrhage.

Materials and Methods: Formerly studied 23 rabbits's documents chosen from our SAH experiments. A control group (Group A) include 5 normal animals, Sham group (Group B) include 5 animals which saline was administered, and a study group (Group C) include 13 animals (7 survive-C1 / 6 dead-C2) which were injected with homologous blood into the cisterna magna. Blood pressure values and and electrocardiograhic changes were recorded per days of all animals before, during and after surgery during two weeks and all animals decapitated under general anesthesia. Hypoglossal nerves, tongue muscles and upper arways were evaluated. Numbers of degenerated axons/neurons density of hypoglossal nerves-atrophic tongue muscles and airway obstruction scores (AOS) of all animals were determined and analysed statistically with ANOVA. AOS was classified according to tongual sliding down distances to larynx numbered between 1-7 mm to scored with 1-7.

Results: Important neurodegeneration was noticed in axons of the hypoglosssal nerves and tongue muscle denervation injury was in more severe in AOS observed animals. The hypoglossal nerves, degenerated axon density (n/mm2), numbers of atrophic muscles (n/mm3) and AOS was: 4±2, 1±1, 1±1 in A; 7±3, 2±1, 2±1 in B and 98±11, 23±5, 5±2 in C1 groups. P values between the axonal degeneration of hypoglossal nerves/muscles and AOS was $p<0.005$ for C2/C1; $p<0.0005$ for C2/A and $p<0.0001$ C2/B.

Conclusion: Hypoglossal ischemia induced tongual muscle palsy related respiratory arrest should be remembered in neurocritical cases. Maintaining normal respiratory functions is only possible with airway tone, which is possible with an intact hypoglossal nerve.

Keywords: Hypoglossal palsy; respiratory disfunctions; subarachnoid hemorrhage

INTRODUCTION

The continuation of respiratory function requires normal airway morphology. Airway obstructions secondary to backwards displacement of the tongue are the most common unpredictible causes of respiratory arrest. Respiratory mechanism ordering craniocervical nerves/ innervating muscles are frequently paralysed and cause airway obstruction during ischemic pathologies. Hypoglossal nerves exit from the hypoglossal canal by perforating the dura mater and descend between the neck fascia and make an ansa hypoglossi network with vagal, trigeminal and the first cervical nerves. That network innervates stylopharyngeal, styloglossus, stylohyoid and intrinsic longitudinal, oblique and transvers muscles of tongue (1). Hypoglossal paralysis occurs after hemispheric

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ischaemia (2), subarachnoid haemorrhage (3). Tongue paralysis due to hypoglossal nerve palsy is a rare but dangerous complication of cerebrovascular diseases because of slipped tongue to larynx (4). Hypoglossal nerve injury cause laryngeal obstruction resulting by tongue swallowing, movement problems, atrophy, deviation (5), fasciculation (6), swelling (7), loss of taste and touch, temperature and somatic sensation of tongue, auditory channels, the pharynx, and the tonsills. Because hypoglossal nerve palsy could be unpredicted airway obstruction, we planned a preliminary study to explain the rational mechanism of mentioned complication.

MATERIALS and METHODS

This study was done of 23 rabbits's documents chosen from our formerly SAH experiments. Following general anesthesia by subcutaneous injection of ketamine (25 mg/kg) hydrochloride were given. A control group include 5 normal animals, sham group include 5 animals which 1 mL saline was administered, and study group include 13 animals (7 survive/6 dead-usually in first week) which were injected with 1mL of autologous arterial blood into the cisterna magna. Blood pressure values and and electrocardiograhic changes were recorded per days of all animals before, during and after surgery during two weeks. CT examination was done and all animals sacrified under general anesthesia. Hypoglossal nerves, tongue muscles and upper arways were evaluated. Surgical dissections were conducted at the Ataturk University Research Laboratory according to ethical committee guidelines. The intracardiac formaline of 10% was injected to formalin-fixed cadaveric rabbits's heads following cardiac arrest. Cadaveric dissections were done under surgical microscope (Carl Zeiss; Oberkochen, Germany) after heads positioning, lateral suboccipital or total transcondylar approache was used to remove of the arch of the atlas. Additionally, occiput and condyles were transected the with petrosal drilling and the posterior part of the hypoglossal canal and the extra/intracranial travels of the nerves to muscles and tongue were exposed. To examine of the extracranial course of the hypoglossal nerves, submandibular incision was done inferiorly across the sternocleidomastoid muscle course from the mastoid tip to the mentum. Anterior border of the sternocleidomastoid muscle dissected and retracted of prevertebral muscles and fascia. Then carotid sheath exposed with the provide of eosephagus and trachea. Deeperly located arteries, nerves and extratongual muscles were explored for to visualize the hypoglossal nerve trajectory and their relationships in tongue.

Normal Microanatomical Features of Hypoglossal Nerves

Hypoglossal nerve nucleus found in the hypoglossal trigone in the medulla oblongata just located in fourth ventricle's floor. Nerve roots arising from the trigone and travel to the root exit zone as radicular fibers and ends at the dural pore. After perforating the dura mater of hypoglossal canal, exit from condylar channels among the vertebral arteries, veins, and posterior inferior cerebellar artery and the as documented by von Luschka in 1867 (8). Hypoglossal nerves exit as two main roots from hypoglossal canal and fused with vagus and accessory nerves. Hypoglossal nerve makes a network with hypoglossal/accessory nerves in the posterior pharyngeal location. After exiting from hypoglossal canal, it descends among the fascia of sternocleidomastoid muscle, internal carotid artery, glossopharyngeus, vagus and accessory nerves. The hypoglossal nerve makes ansa hypoglossi with branches of vagal, trigeminal and the first cervical nerves. Before reaching common carotid artery bifurcation, the descending branches of hypoglossal nerves make ansa cervicalis. Then, it reaches the stylopharyngeal, styloglossus, stylohyoid and intrinsic longitudinal, oblique and transvers muscles of tongue described by Iaconetta G and Ates S (1, 9).

Airway obstruction scores (AOS)

AOS was classified according to tongual sliding down distances to larynx. Distance is measured with a ruler which scale 0-10 mm.

Statistical Analysis

Statistical analysis was performed with SPSS Statistics version 22.0 (IBM, Armonk, NY, USA). Normal distribution of data was assessed with the Kolmogorov–Smirnov or Histogram test. Continuous variables were expressed as mean (standard deviation) (SD). Numbers of degenerated axons/neurons density of hypoglossal nerves-atrophic tongue muscles and airway obstruction scores (AOS) of all animals were determined and analysed with the One-Way ANOVA for independent variables. The Kruskal Wallis test was used for the non-normality distributed data. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Pathoanatomical and Histopathological Features of the Study

Figure-1 shows computerised tomographical appearances of craniocervical region, tonsillary herniation and upper airway obstruction. Macroscopical view of posterior craniocervical region brain with a SAH created rabbit. Histopathological appearances of hypoglossal nerve in SAH created basal cistern (Figure-2). Figure-3 shows microscopical view of hypoglossal nerve roots just entering to hypoglossal channel in a bloody subarachnoid space and degenerated axons of hypoglossal nerves.

Numerical Results

Prominent neurodegeneration detected in hypoglosssal nerve axons and tongue muscle denervation injury was in more severe in AOS observed animals. The degenerated axon density of hypoglossal nerves (n/mm2), numbers of atrophic muscles (n/mm3) and AOS was: 4±2, 1±1, 1±1 in group A; 7±3, 2±1, 2±1 in group B and 98±11, 23±5, 5±2 in group C1. P values between the axonal degeneration of hypoglossal nerves/muscles and AOS was $p<0.005$ for C2/C1; $p<0.0005$ for C2/A and $p<0.0001$ C2/B. the

statistical differences between degenerated axon density and atrophic muscles was parallel with our statistical results. Numerical results are given on Table 1.

Table 1. Numerical statistical values of study

	Group A (n=5)	Group B (n=5)	Group C (n=13)	
DADHN (n/mm²)	4±2	7±3	98±11 α, β, γ	112±15 β, γ
Numbers of atrophic muscles (n/mm³)	1±1	2±1	23±5 α, β, γ	40±8 β, γ
AOS (mm)	1±1	2±1	5±2 α, β, γ	6±1 β, γ

Group A; Control, Group B: Sham, Group C: Study, C1: Survive, C2: Death
DADHN: Degenerated axon density of hypoglossal nerves.
α p < 0.005 between C2 and C1
β p < 0.005 between C1,C2 and A
γ p<0.0001 between C1,C2 and B

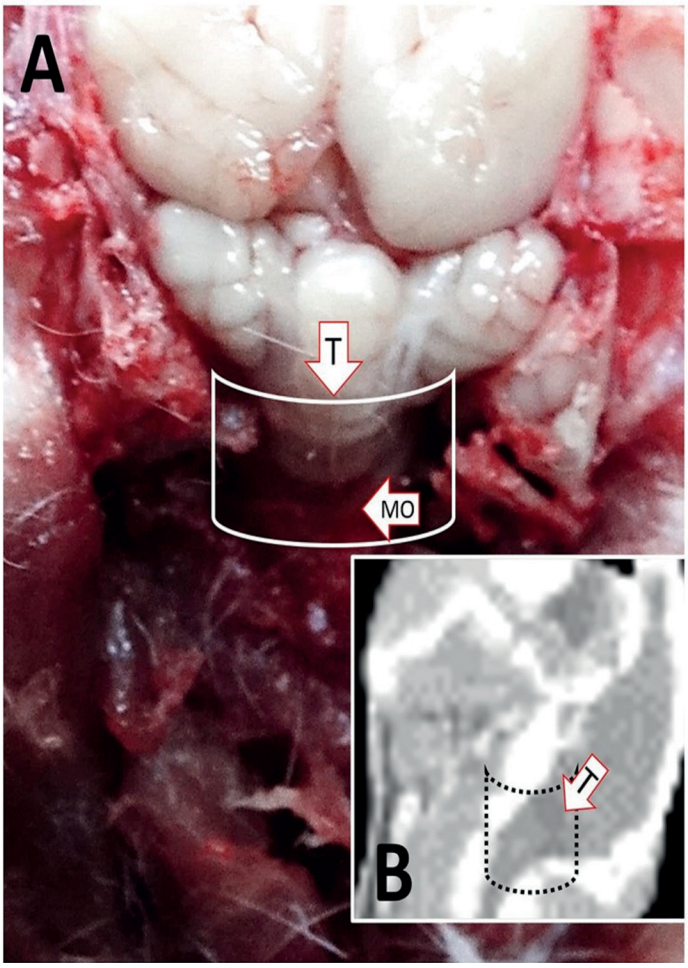

Figure 1. Anatomical appearence of cerebellum and herniated tonsil part (T) above the medulla oblongata (MO) following posterior fossa craniectomy (A), Magnified form of cranium with tonsillary herniation (black arrow) (B).

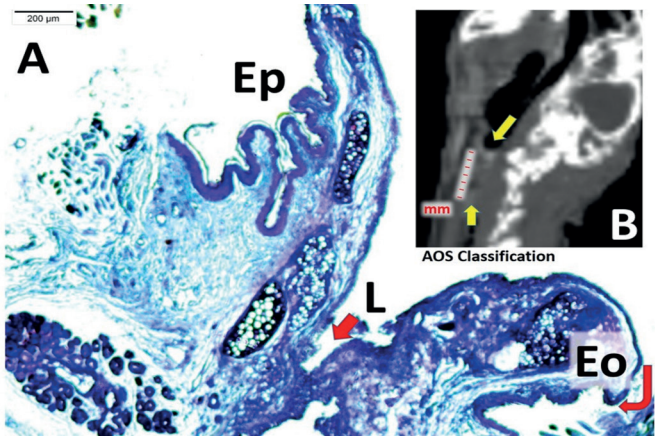

Figure 2. Histopathological view of epiglottis (EP), obstructed larynx (L), edematous laryngoeosephageal valv and posteriorly distructed eosephageous (EO) is seen in a dead rabbit secondary to hypoglossal palsy detected animal (LM, MTC, x 4) (A), CT appearence of pharyhngolaryngeal region, collapsed pharyngolaryngeal tissues (yellow arrows) with milimetric ruler (B)

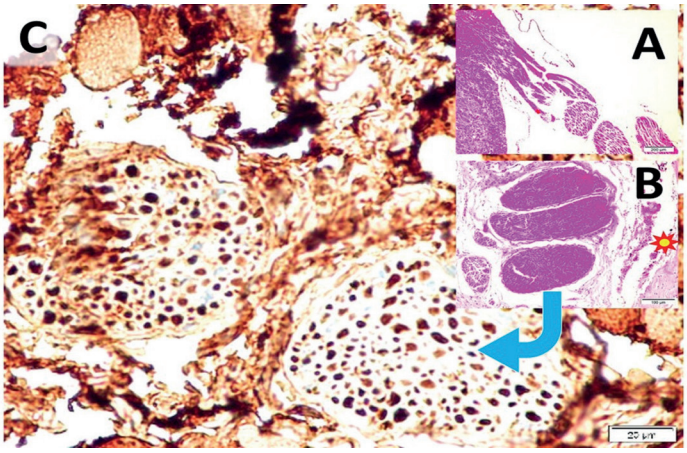

Figure 3. Histopathological appearence of sagittal section of hypoglossal nerve (LM, H&E, x4) (A), horizontal section (LM, H&E, x10) (B), normal (tick-points) and degenerated (thin-points) axons of hypoglossal nerves (LM, GFAP, x40) (C) of are seen in a dead rabbit secondary to hypoglossal palsy detected animal

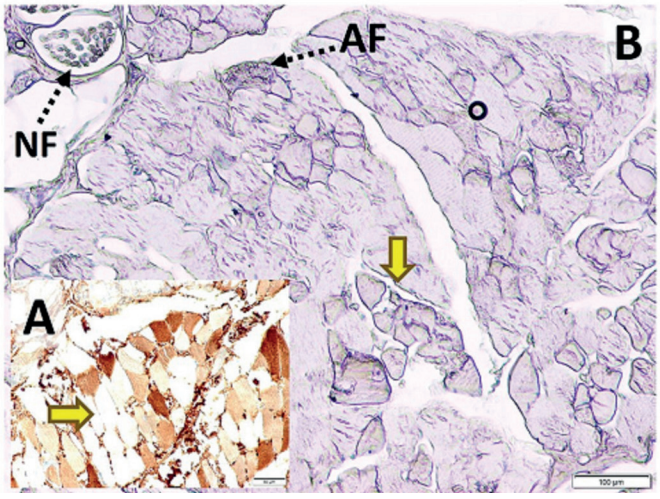

Figure 4. Histopathological view of normal tongual muscles (dark) with nerve fibers as brownish points and atrophic tongual muscles (clear) (A); normal fibers (NF) and apoptotic fibres (AF), apoptotic tongual muscles (yellow arrow) (LM, Tunel x 10) (B) are seen in a dead rabbit

DISCUSSION

The first condition for the functional continuity of the respiratory function is that the airways have normal morphology. Airway obstructions, which are caused by the displacement of the tongue backwards, are the most common causes of respiratory arrest, but it frequently ignored. Craniocervical nerves indispensable for respiratory mechanics are often kept in combination during ischemic pathologies. Regardless of the consciousness, mechanical obstruction result from the backward sliding of the tongue to larynx owing to hypoglossal and neighbor cranial nerves palsy should not be forgotten following subarachnoid hemorrhage. Because some important anatomical and functional relations for respiration among craniocervival nerves can be disrupted and their innervating muscles paralysis could relay on upper airway obstruction during subarachnoid hemorrhage (10).

Hypoglossal nerve arising from the posterolateral side of the trigonum hypoglossi located in the base of the fourth ventricle and go through toward the root exit zone as radicular fibers and ends at the dural pore. The hypoglossal nerve connects to the branches of vagal, trigeminal and the first cervical nerves and forms ansa hypoglossi to innervate oropharyngolaryngeal muscles (1). The nerve sent branches to the styloglossus, hyoglossus, genioglossus and geniohyoideus muscles and terminated in the intrinsic tongue muscles (9). Autonomic fibers of ansa hypoglossi innervate craniocervical arteries, ganglia, muscles, and secretory glands (11). Motoneurons of hypoglossus innervate intrinsic and extrinsic tongue muscles (12).

The tongue plays an important role in both swallowing and breathing (13). Hypoglossal nerves may influence the respiratory rhythm (14). Rhythmical masticatory activity can be beginning of hypoglossal motoneurons induced by oral stimulus (15). Medial branch of hypoglossal nerve stimulation reduces airway resistance induced by functional airway obstruction (16).

Hypoglossal nerve injury may result in swallowing (5). Ipsilateral hypoglossal nerve palsy may occur following left hemithyroidectomy (17). Hypoglossal nerve injury cause muscle denervation pathologies of tongue (18). Isolated paralysis of hypoglossal nerve is uncommon (19). Lingual paralysis ocur after unilateral upper motor neuron lesions after monohemispheric ischaemia (2). Hypoglossal nerve palsy may be asssociated with subarachnoid haemorrhage (3). Also, sympathetic and parasympathetic function abnormalities frequently occur together with in some cases. Hypoglossal nerve palsy presented with tongue swelling (7). Hypoglossal nerve dysfunctions cause respiratory depression and upper airway obstruction during sedation and anesthesia (20). Hypoglossal nerve palsy leads to marked muscle atrophy of tongue (21). Lingual motor deficits cause swallowing difficulties and pulmonary aspiration (13).

Critical relationship between the lower cranial nerves mostly affected craniaocervical lesions and play major roles in combined syndromes uch as Collet-Sicard syndrome presented with hoarseness, swallowing difficulties and dysphagia (22). Carotid artery (23), vertebral artery (24), aneurysms, and extensive craniocervical pneumatization (25), hypoglossal schwannoma (26), persistent primitive hypoglossal artery (27), gunshot wounds, stroke, hysteria, multiple sclerosis, Guillain-Barré neuropathy (28), infection and irradiation (29) cause glossopharyngeal, hypoglossal and trigeminal nerve injuries. Isolated hypoglossal nerve palsy is seen in atlanto-occipital synovial cyst and fractures (30). All physicians should be aware of in such stuations in view of hypoglossal palsy induced acute respiration difficulties.

Rationale of that study

Tongue is an interesting detector which regulates between the internal and external milieu changes. Hypoglossal palsy not only cause motor deficit but also taste, oral pH and mechanosensitive sense abnormalities of tongue. Superficial and deep sensorial reflexes of swallowing, chewing, vomiting, and respiration is essentially regulated by tongue. For, nutrition, digestion, immunity, and vital functions require normal functioned tongue. Thus, tongue palsy leads to weakness in metabolic and endocrine functions.

Limitation

This study aims to investigate hypoglossal nerve damage as a cause of mechanical airway obstruction in subarachnoid hemorrhages. We did not encounter similar or opposite forms of this study in the literature, which we hypothesized as a preliminary study. After this study, there is a need for experimental and clinical studies with large series, including radiological imaging. This was the major limitation of the study.

Clinical importance of the presented study

Unexpected respiratory arrest in urgent; chewing-swallowing and speech abnormalities; and, metabolic disorders should be considered as late complications of subaracnoid hemorrhage. Intraoperative hypoglossal nerve mapping should be done during carotid endarterectomy (31). Hypoglossal stimulation used in treatment of obstructive sleep apnea syndrome (32).

CONCLUSION

Mechanical respiratory arrest owing to upper airway obstruction with tongual paralysis induced by hypoglossal nerve paresia/palsy during subarachonoid hemorrhage shold be considered as a causative factor on development of mechanical respiration arrest which has been mentioned in the literature so far.

Future insight

Today, many patients breathe spontaneously at the time of admission to intensive care units. These patients are intubated under elective conditions in case of any regression in their state of consciousness during their

follow-up and treatment by the basic intensive care principles. Subarachnoid hemorrhage is a common clinical condition in intensive care patients regardless of the reason for hospitalization. It often progresses with impaired consciousness, causing patients to be intubated.

Hypoglossal nerve damage is common in subarachnoid hemorrhage cases, regardless of impaired consciousness. Loss of tongue tone due to this damage results in the tongue's posterior displacement, which is the most common cause of airway obstruction. During intubation, the tongue is the first element to be eliminated, which may cause it to be overlooked that airway obstruction results from hypoglossal nerve damage.

Therefore, subarachnoid hemorrhage and related hypoglossal nerve damage should be kept in mind in patients with respiratory depression. During the weaning preparation process of these patients, evaluating a tongue tone that is enough to keep the airway open is as important as other lung examinations.

Competing interests: The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports.

Ethical approval: Ataturk University Laboratory Animal Ethical Board.

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