Glossopharyngeal Neuralgia Associated with Bradycardia, Syncope, and Seizures

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The syndrome of glossopharyngeal neuralgia associated with disturbances of cardiac and cerebral function is a rare disorder, having been reported to our knowledge in only 16 patients. It is characterized by paroxysms of neuralgic pain in the throat and neck and accompanied by bradycardia or asystole, hypotension, syncope, and sometimes seizures. The following report describes detailed cardiovascular and neurologic studies of a patient with this syndrome who responded satisfactorily to treatment with diphenylhydantoin (Dilantin).

Case History

A 72-year-old Negro was admitted to the hospital for the first time in February 1963. He had been seen as an out-patient 10 years previously, when he complained of frequent paroxysms of severe pain in the angle of the mandible below the right ear. A diagnosis of glossopharyngeal neuralgia was made and surgical section of the ninth cranial nerve was recommended. His symptoms disappeared spontaneously within a few weeks, however, and he did not return for this operation.

He remained completely free from pain for approximately 2 years. The pain then recurred in clusters at irregular intervals, lasting for as long as a few weeks to a few months, with remissions varying from several months to a year or more.

In November 1962, the patient developed a severe exacerbation of the neuralgia. The pain was aggravated by cold weather and was frequently precipitated by swallowing ice or cold liquids. Other foods or liquids also produced pain and the patient attempted to swallow on the left side of the throat to avoid stimulating the right palatopharyngeal area. The pain usually appeared five or six times a day, lasting for perhaps 20 seconds. At times, however, he had as many as 10 to 20 attacks a day.

In the 2 months prior to hospital admission, the paroxysms of pain were associated with faintness and occasional loss of consciousness with convulsive movements. The patient almost always developed syncope if the pain occurred when he was sitting or standing, but only a transitory sensation of faintness was noted while recumbent. Syncope never occurred without an associated episode of pain. The patient estimated that he had fainted a dozen times. There were no other neurologic manifestations such as paralysis, headaches, speech defects, or hearing loss. There was likewise no history to suggest cardiac, pulmonary, or gastrointestinal disorders.

Physical examination revealed no abnormalities except the cardiovascular changes accompanying the paroxysms of pain. Complete blood count and urinalysis were normal. The fasting and 2-hour postprandial blood sugars were 126 and 140 mg. per cent, respectively. A glucose tolerance test showed impaired tolerance with return to fasting blood sugar levels in 4½ hours. The blood urea nitrogen level ranged from 25 to 35 mg. per cent. Roentgenograms showed hypertrophic arthritic changes of the cervical spine; the chest, abdomen, and skull were normal. Electrocardiograms were normal except for first-degree heart block and nonspecific T-wave changes. The electroencephalogram was normal for a patient of his age.

Cardiovascular Changes

The electrocardiogram and intra-arterial blood pressure were monitored during spontaneous paroxysms of pain as well as during induced attacks of neuralgia. The onset and ending of each paroxysm of pain were indicated by the patient with an electrical signal on the record. The onset of each episode of pain was followed invariably within 3 or 4 seconds by a decrease of heart rate from 80 to 90 per minute to 45 to 50 per minute and a fall of blood pressure from approximately 140/70 to 80/40 mm. Hg (fig. 1). P-wave changes were also observed in the electrocardiogram, indicating a shift of the pacemaker from the sinoatrial node to the lower atrium. These
When however, were noticed faintness during the attack and the bradycardia only lasted 10 to 15 seconds. The appearance time and mean circulation time were definitely prolonged during the attacks with an increase from 8.5 to 10 seconds, and from 14.9 to 17.2 seconds, respectively. During the paroxysms of pain, the ballistocardiogram showed increased amplitude of all components, but the basic pattern remained unchanged.

These cardiovascular and neurologic manifestations not only occurred spontaneously but also could be induced by swallowing ice or mechanical stimulation of the trigger zones on the right side of the pharynx. Massage of either carotid sinus failed to produce any pain or bradycardia. Somatic pain induced by compression of the Achilles tendon likewise had no effect on the heart rate or blood pressure. The patient responded to Valsalva maneuvers normally and had no significant blood pressure changes on head-up tilt to 60 degrees. During the experimental observations there were two occasions in which mild bradycardia developed in the absence of neuralgia.

Changes lasted for approximately 15 seconds, subsiding shortly before the pain completely disappeared. When in the upright position, the patient noticed faintness during the attack but no electroencephalographic abnormalities were observed.

The cardiac output, as estimated by indocyanine dye-dilution method showed no significant change during the attacks. These determinations, however, were of questionable validity, since the heart rate was changing constantly during the attacks and the bradycardia only lasted 10 to 15 seconds. The appearance time and mean circulation time were definitely prolonged during the attacks with an increase from 8.5 to 10 seconds, and from 14.9 to 17.2 seconds, respectively. During the paroxysms of pain, the ballistocardiogram showed increased amplitude of all components, but the basic pattern remained unchanged.

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Effects of Pharmacologic Agents

Observations were made on the effects of atropine. Following the intravenous injection of 1.2 mg. of atropine, the heart rate increased from 82 to 145 per minute. During this period the patient continued to have spontaneous and induced attacks of neuralgia, but without bradycardia, hypotension, or syncope. As a result of these observations, atropine, 0.2 mg. was administered subcutaneously four times a day. Unfortunately the patient developed confusion and disorientation with this dosage of atropine, and the treatment was discontinued.

The patient's neuralgic attacks were also observed during tachycardia induced by a sympathomimetic drug. Isoproterenol was given intravenously at a constant rate of 0.49 mcg. per minute. After a total dose of 42 mcg, the heart rate increased from 80 to 120 per minute. Despite this degree of tachycardia the patient continued to have spontaneous attacks of neuralgic pain and bradycardia of the same magnitude (45 beats per minute). These attacks occurred 14 times during a 30-minute period.

Local anesthesia produced by applying lidocaine (Xylocaine) to the mucous membranes of the oropharynx failed to prevent the spontaneous paroxysms of pain and bradycardia. This measure, however, blocked the induction of pain by swallowing or by mechanical stimulation of the trigger zone.

A glossopharyngeal nerve block was attempted by injection of 6 ml. of mepivacaine (Carbocain) in the area of the right jugular foramen. The

Figure 1

Simultaneous records of electrocardiograms and intra-arterial pressure tracing during a spontaneous attack of glossopharyngeal neuralgia showing the bradycardia, fall of blood pressure, and the P-wave changes of electrocardiogram.
patient developed a transient right facial weakness, paralysis of the right side of the palate, and deviation of the tongue, indicating block of the seventh, tenth, and twelfth cranial nerves as well. The neuralgic pain and bradycardia, which had previously recurred at intervals of approximately every 2 minutes, were completely abolished for a period of an hour. When the effect of the anesthesia had disappeared, the pain and bradycardia returned as previously experienced.

The effects of diphenylhydantoin (Dilantin) were also studied. This medication in doses of 300 and 400 mg. a day had no effect on the attacks. He became completely free from pain, however, after the dosage was increased to 500 mg. a day. During treatment with diphenylhydantoin, continuous monitoring of the heart rate with radiotelemetry failed to reveal any episodes of bradycardia. Swallowing of ice and stimulation of the trigger zone likewise failed to produce either the paroxysms of pain or bradycardia. Substitution of placebo medication for diphenylhydantoin was followed in 4 days by recurrence of pain, bradycardia, and syncope with as many as 47 attacks in 12 hours. Restoration of therapy was again followed by cessation of pain on the second day.

Following discharge from the hospital the patient remained symptom-free for 6 months during which he received 500 mg. of diphenylhydantoin a day. He then developed symptoms of toxicity, manifested by ataxia, nystagmus, and dysmetria, but there was no pain or syncope. Neither neuralgia nor bradycardia could be induced by swallowing or stimulation of the trigger area. Following the substitution of placebo for diphenylhydantoin the patient again experienced glosopharyngeal pain, but bradycardia or syncope did not recur. After the symptoms of drug toxicity had subsided, this therapy was re-instituted at the dosage of 300 mg. a day. This dosage was well tolerated and the patient had no bradycardia, dizziness, or syncope; there was a marked decrease in severity of the neuralgia.

**Discussion**

The mechanism by which glosopharyngeal neuralgia produces cardiac and cerebral manifestations is not completely understood. It is not the usual vasovagal reaction to pain, because the somatic pain from other areas of the body did not produce similar changes of blood pressure or heart rate. It is not due to hypersensitivity of the carotid sinus, as massage of the sinuses in our patient and in most of the reported cases failed to reproduce the typical cardiovascular manifestation of this syndrome. It has been suggested, however, that the vagus nerve or the carotid sinus reflex arc is responsible for the bradycardia and hypotension. This is supported by the fact that the cardiovascular changes can be completely abolished with parasympathetic-blocking agents such as atropine, but not with a sympathomimetic agent, i.e., isoproterenol.

The cardiovascular changes in our patient did not appear until 3 or 4 seconds after the onset of pain, and occurred only when the pain was most intense; the changes were not present when the pain was modified by diphenylhydantoin therapy. It would appear that only pain of certain severity activates the "glosopharyngeal-vagal reflex arc," resulting in bradycardia, hypotension, and syncope. It has been suggested that intense afferent impulses from the sensory fibers of the glosopharyngeal nerve may stimulate the dorsal motor nucleus of the vagus nerve either by way of central collateral pathways or through an "artificial synapse" along the peripheral course of the glosopharyngeal nerve as it travels with the nerve of Hering.

The changes in cerebral function are generally considered to be caused by transient cerebral ischemia secondary to bradycardia and hypotension. However, Thomson reported one patient in whom syncope and convulsions occurred during the paroxysm of glosopharyngeal neuralgia in the absence of a fall in heart rate or blood pressure. It was suggested that such patients might have a "cerebral type" of carotid sinus syncope as described by Weiss. In our patient, the degree of slowing of the heart rate was minimal but there was a rather marked hypotension with associated syncope. This suggests that there may be other factors present in this individual, such as arteriosclerotic vascular disease, which make him much more susceptible to the effects of even minor reductions in heart rate and in blood pressure.

Although local anesthesia and nerve block may relieve the neuralgia, and atropine may abolish the cardiovascular symptoms, the effects of these measures are temporary. Intra-

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cranial section of the glosopharyngeal nerve has been most successful in this condition,\textsuperscript{16–20} but occasionally resection of the rostral two rootlets of the vagus nerve is necessary to produce complete remission of the neuralgia.

Diphenylhydantoin therapy was employed in our patient, since this medication has been found to be effective in trigeminal neuralgia. In such patients it raises the threshold of the neuralgic pain, shortens the duration of the paroxysm, and frequently abolishes the attacks.\textsuperscript{21} The use of this medication in glosopharyngeal neuralgia has been reported in only four patients. One patient had satisfactory response,\textsuperscript{22} another had transient relief for about 10 days, but the two remaining patients had no response.\textsuperscript{12, 14} In our patient, the symptoms were completely relieved by diphenylhydantoin but only with high doses. The pain and bradycardia recurred on placebo therapy and subsided again with readministration of the medication. These observations indicate that diphenylhydantoin is effective in this condition and also support the experience of Iannone et al.\textsuperscript{22} that trigeminal and glosopharyngeal neuralgia can be modified with small doses of this agent and completely abolished with large doses.

**Summary**

An unusual case of glosopharyngeal neuralgia associated with bradycardia, hypotension, syncope, and seizure is described. Our observations indicate that the cardiovascular components of this syndrome are probably due to stimulation of vagal centers by pain impulses arising from the glosopharyngeal area. Diphenylhydantoin therapy produced satisfactory relief of symptoms in this patient, probably by modification of the intensity of the neuralgic pain and thereby reducing the central vagal response.

**References**


Reports of Medical Cases, with Reference to Morbid Anatomy Preface by Richard Bright—1827

Where anasarca has come on from exposure to cold, or from some accidental excess, I have in general found the urine to be coagulable by heat. The coagulation is in different degrees: it likewise differs somewhat in its character; most commonly when the urine has been exposed to the heat of a candle in a spoon, before it rises quite to the boiling point it becomes clouded, sometimes simply opalescent, at other times almost milky, beginning at the edges of the spoon and quickly meeting in the middle. In a short time the coagulating particles break up into a flocculent or a curdled form, and the quantity of this flocculent matter varies from a quantity scarcely perceptible floating in the fluid, to so much as converts the whole into the appearance of curdled milk. Sometimes it rises to the surface in the form of a fine scum, which still remains after the boiled fluid has completely cooled. There is another form of coagulable urine, which in my experience has been much more rare; when the urine on being exposed to heat assumes a gelatinous appearance, as if a certain quantity of isinglass had been dissolved in water. I have indeed met with this in one or two cases only.—Original Papers of Richard Bright on Renal Disease. Edited by A. ARNOLD Osman. London, Oxford University Press, 1937, p. 3.
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