

Nasopharyngeal Carcinoma Mimicking a Temporomandibular Disorder: A Case Report

Shoshana Reiter, DMD
Instructor

Anat Gavish, DMD
Lecturer

Ephraim Winocur, DMD
Lecturer

Alona Emodi-Perlman, DMD
Instructor

Ilana Eli, DMD
Professor

Department of Oral Rehabilitation
The Maurice and Gabriela Goldschleger
School of Dental Medicine
Tel Aviv University
Tel Aviv, Israel

Correspondence to:

Dr Shoshana Reiter
The Maurice and Gabriela Goldschleger
School of Dental Medicine
Tel Aviv University
Tel Aviv, Israel
E-mail: shosh5@bezeqint.net

Patients referred from an otorhinolaryngologist with a chief complaint of earache or other ear symptoms are common in a temporomandibular disorders (TMD) clinic. These patients often complain of other symptoms, such as headache, facial pain, and limited mouth opening, all of which can be present in a patient suffering from a nasopharyngeal carcinoma (NPC). The aim of this case report was to describe the signs and symptoms of NPC and discuss possible causes for the misdiagnosis of NPC as TMD. The characteristics of 8 NPC patients reported in the literature whose cancer was initially misdiagnosed as TMD and those of an NPC patient with TMD-like symptoms treated at the clinic of 1 of the authors are described, and the reasons for misdiagnosis are discussed. A revision of Trotter's syndrome for the differential diagnosis of TMD is proposed. There is a need for detailed exclusion criteria to be applied prior to the assignment of a clinical diagnosis based on the Research Diagnostic Criteria for TMD. J OROFAC PAIN 2006;20:74-81

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Nasopharyngeal carcinoma (NPC) originates in the nasopharyngeal epithelium. In the United States, the annual incidence of NPC ranges from 0.2 to 0.5 per 100,000 inhabitants. The highest incidence rate of NPC, 24.3 per 100,000 inhabitants, is reported among the population of southern China.¹ Intermediate rates are found in Southeast Asia, North Africa, and parts of the Middle East.¹⁻⁵ NPC can occur at any age but the incidence increases with age in most low-risk populations. However, the incidence peaks between 15 and 25 years in high-risk populations.^{1,6} The male-female ratio of NPC is approximately 2:1 or 3:1 in most parts of the world.¹ The pathogenesis of NPC is not fully understood and is considered multifactorial, with genetic factors, Epstein-Barr virus, and dietary factors being the most important risk factors.⁷

For an early diagnosis of NPC, it is important to realize that early signs and symptoms are subtle,⁸ and are sometimes unnoticed even by the patient. Some of these early and mid-stage signs

Table 1 Signs and Symptoms of NPC in the Early, Middle, and Advanced Stages^{9,14,15}

Early stage	Middle stage	Advanced stage	Other signs and symptoms*
<ul style="list-style-type: none"> •Auditory complaints: plugging, drainage, tinnitus, deafness/ decreased hearing, dizziness •Asymmetry of the soft palate •Low-grade facial pain that is dull, aching, or pressing 	<ul style="list-style-type: none"> •Severe hard-end limitation of mouth opening •Contralateral deviation upon mouth opening •Ipsilateral sensitivity to palpation •Pain increased with function •Pain more severe and continuous 	<ul style="list-style-type: none"> •V Cranial nerve involvement: trigeminal neuralgia, denervation atrophy of muscles of mastication, numbness •VI Cranial nerve involvement: ophthalmoplegia, visual changes •XII Cranial nerve involvement: deviation of tongue upon protrusion •Cervical lymph node involvement: Ipsilateral or bilateral neck masses •Other metastasis with associated signs and symptoms: liver, spine, brain, lung, bone, axillary lymph nodes 	<ul style="list-style-type: none"> •Headache •Neck ache •Nasal obstruction •Epistaxis •Vertigo •Nausea •Persistent sore throat/foreign body sensation •Fatigue •Weight loss

*The stage in which these signs and symptoms first appear has not yet been established.

and symptoms, eg, facial pain, limited mouth opening, jaw deviation upon opening, earache and headache, could be mistaken for signs of a temporomandibular disorder (TMD).⁹ Therefore, the orofacial pain clinician and the general dentist can play an important role already at these stages in order to provide an early diagnosis.¹⁰ While some symptoms, such as ear plugging, tinnitus, decreased hearing, and deafness appear early, cervical neck masses (ie, enlarged lymph nodes), trigeminal neuralgia,¹¹ denervation/atrophy of the masticatory muscles,¹² and facial numbness and other cranial nerve deficits (especially of cranial nerves V and VI) represent advanced stages that are caused by the intracranial spread of the tumor¹³ (Table 1). Based on such diverse signs and symptoms, diagnosis of this malignancy is difficult, and therefore, delayed diagnosis (6 to 9 months) is common.¹⁰ An early diagnosis of the malignancy is crucial, as the 5-year survival rate decreases dramatically in advanced stages, ie, from 76% when the tumor is confined to the nasopharynx to 43% when it extends into the prestyloid and pterygopharyngeal space.¹⁶

Dr Wilfred Trotter was the first¹⁷ to recognize the unique early clinical presentation of NPC in 1911. Without the sophisticated techniques available today, Dr Trotter managed to characterize the NPC patient profile in the early stages of the disease based on a superb diagnostic approach as well as the signs and symptoms of only 14 patients. He noted that the tumor tends to develop close to the eustachian tube opening, causing decreased hearing. Later, the tumor extends to the most proximal anatomic site, the levator palati muscle, causing defective mobility of the soft palate on that side. Further tumor progression involves the ipsilateral mandibular branch of the trigeminal nerve, caus-

ing severe pain in the ear and along the temple, mandible, and tongue that was diagnosed in his time as trigeminal neuralgia. Further progression involves the medial pterygoid muscle, which lies external to the aforementioned structures, causing limited mouth opening. Trotter stated that “owing to the nearness to one another of the structures involved, symptoms so diverse as deafness, trigeminal neuralgia and an affection of the palate might be produced by a lesion no larger than a walnut.”¹⁷ Trotter also noted that enlargement of cervical lymph nodes is a constant feature in late stages and that the tumor has a tendency to extend intracranially through the foramen ovale and involve the gasserian ganglion, causing sensory alterations in the face.¹⁷

The purpose of this article is to describe the NPC signs and symptoms in order to prevent misdiagnosing this condition as TMD. This description is based on the review of 8 NPC cases found in the literature that had been misdiagnosed as TMD and on the characteristics of a new case. A revision of Trotter’s syndrome is proposed based upon current understanding of orofacial pain mechanisms.

Case Report

A 14.5-year-old white male adolescent was referred by an otorhinolaryngologist to a TMD clinic in northern Israel with the chief complaints of a sudden onset of earache, plugging, and decreased hearing in the left ear. His symptoms had started about 1.5 months before (Table 2). Limited mouth opening was the only finding of the otorhinolaryngologist. No audiogram was taken,

Table 2 Summary of Cases Described in the Literature

Study	Age (y)	Gender	Chief complaint	Ear signs and symptoms	Range of motion	Pain characteristics	Pain intensity	Pain site (by patient)	Neurologic symptoms	Neurologic evaluation	Final diagnosis
Present case	14.5	M	Plugging of left ear, decreased hearing	Plugging, decreased hearing in left ear	23–25 mm	Dull, aching, aggravated by jaw movement	Initially mild, then progressively severe and continuous	Left ear, preauricular and posterior digastric area	None	None	NPC
DeiBalso et al ¹⁸	12	M	Progressive trismus, decrease in acuity in right ear and frequent epistaxis	Decreased acuity in right ear	10 mm	Not described	Not described	Not described	Not described	Not described	Undifferentiated NPC
Cohen and Quinn ¹⁹	16	M	Trismus, right facial pain, occasional ringing in right ear, numbness in right molar region, 40 lb weight loss	Occasional ringing in right ear	6 mm	Intermittent	Severe	Right frontal, temporal, and molar regions	Continuous numbness in right molar area	Examination with no findings	Poorly differentiated NPC
Roistacher and Tanenbaum ²⁰	27	M	Intermittent left ear pain and stuffiness, left facial pain and limited mouth opening	Intermittent left ear pain and stuffiness	Limited opening, condylar translation < 20 mm	Sharp, intermittent, aggravated by jaw movement	Not described	Left ear, preauricular and masseteric region	Numbness of left side of tongue at a later stage	Comprehensive medical workup negative	Epidermoid carcinoma of the nasopharynx
Epstein and Jones ⁹	23	F	Persistent left side facial pain; pain in left occipital area	External otitis; developed lymphadenopathy after 5 mo	Not described	Persistent	Not described	Left facial and occipital areas	Not described	Not described	NPC
Ong and Tan ²¹	9	M	Right temporal, ear and mastoid pain	Earache (initially diagnosed as otitis media)	Marked trismus	Not described	Not described	Right temporal, ear, and mastoid areas	Not described	None	NPC
Trumpy and Lyberg ²²	45	M	Intermittent moderate hearing loss and right facial pain	Right middle ear effusion with moderate conductive hearing loss	< 20 mm	Sharp	Severe, later continuous	Right side of face and neck, centered around TMJ	Not described	Examination with no findings	NPC
Okeson ²³	54	F	Pain in the left ear and preauricular area spreading to the temple, face, and submandibular triangle, and restricted mandibular movement	At first, left eustachian blockage; ear pain thereafter	18 mm	Continuous variable protracted steady dull aching aggravated by 13 mm opening	Mild pain that gradually increased and became severe and continuous	Left ear and preauricular area, spreading to temple, face, and submandibular triangle	Marked anesthesia and paresthesia on left side of face	Referred to neurologist prior to final diagnosis	NPC
Sharav and Feinsod ²⁴	52	F	Pain in right maxillary area radiating to right ear and occipital areas	Right ear pain; later hearing loss in right ear	33–37 mm	Pulsating	Strong, developing rapidly, subsiding within 10 to 15 min	Right maxillary area radiating to right ear and occipital area	Occasional tingling and numbness of right cheek, palate, and maxillary teeth	Mild hypoesthesia in the second division of right trigeminal nerve	Adenocarcinoma of the nasopharynx

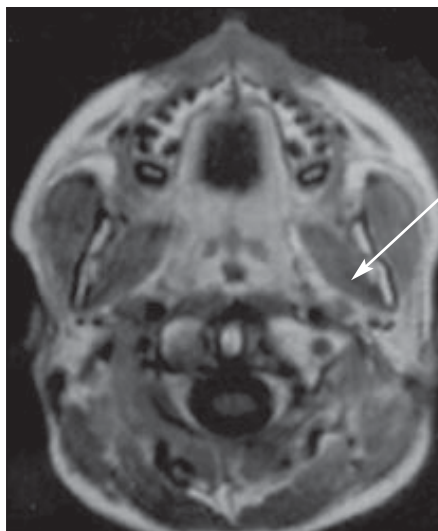
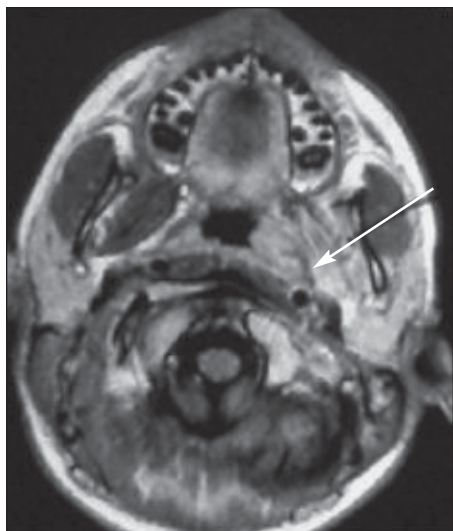


Fig 1 (left) MRI of the patient prior to therapy showing loss of image of the left medial pterygoid muscle (*arrow*).

Fig 2 (right) MRI of the patient following irradiation and chemotherapy. Arrow indicates restored image of the left medial pterygoid muscle.

and the patient was referred to a TMD clinic. On examination at the TMD clinic, the patient reported pain in the left ear and preauricular and digastric areas. Active mouth opening was restricted to 23 mm with a marked deviation of the mandible to the right. Maximum opening could be passively increased slightly (to 25 mm) and was associated with an increase in pain. The pain was described as dull, aching, and unilateral (left) and was associated with the opening movement. The patient tended to dismiss the pain as “nothing much.” There were no joint sounds during palpation nor was there joint tenderness. However, there was mild tenderness of the left anterior temporalis and masseter muscles, and the left posterior digastric area was very sensitive to palpation. A hard and tender lymph node, the size of a pea, was palpated in the left superior deep jugular area. Oral and dental examinations were noncontributory. Panoramic radiograph showed both temporomandibular joints (TMJs) to be structurally normal, with no additional pathology. There was no history of trauma or parafunction, and the medical history was noncontributory.

Clinical examination using the Research Diagnostic Criteria for TMD²⁵ (RDC/TMD) excluded a TMD. Therefore, the patient was referred to an oral surgery clinic for further evaluation. Physiotherapy was recommended. Because the patient’s symptoms progressed further, he was referred for a computerized tomographic (CT) scan, which failed to show the tumor. Two months later, he was diagnosed with NPC based on a new otolaryngological examination and magnetic resonance imaging (MRI) findings (Figs 1 and 2).

Summary of the Cases Reported in the Literature

The characteristics of 8 cases reported in the literature in which NPC was originally thought to be TMD are reported in Table 2. Several features were found to be common in this sample.

Age and Gender

The patients were either young ($n = 6$; range, 9 to 27 years) or middle aged ($n = 3$; range, 45 to 54 years). The male:female ratio was 6:3.

Severe Limitation of Mouth Opening

Five patients^{18–20,22,23} had mouth opening of less than 20 mm, 1 patient (the present case) has mouth opening of 23 to 25 mm, and 1 patient²⁴ had mouth opening of 33 to 37 mm. In 1 patient the severe limitation was described as “marked trismus,”²¹ and the opening range was not described for the remaining patient.⁹ Restricted mouth opening was accompanied by marked deviation to the contralateral side in 2 patients,²³ including the present case.

Ear Symptoms

All patients reported ear symptoms. This was part of the chief complaint in 8 of 9 patients. External otitis developed 5 months after initial presentation in 1 patient,⁹ and decreased hearing developed at a later stage in another patient.²⁴ The most common ear complaints were ear pain ($n = 4$) and decreased hearing ($n = 3$).

Site of Pain

Pain location was described for 8 patients. In 4 patients,^{20,22,23} including the present case, pain was located in proximity to the TMJ; it spread to the ear in 1 patient.²⁴ The posterior digastric area was the main pain site in 1 patient (the present case). Pain was located in the maxillary area in another patient,²⁴ in the occipital area in 2 patients,^{9,24} in the frontal area in 1 patient,¹⁹ in the mastoid area in 1 patient,²¹ and in the ipsilateral neck area in another patient.²² The temporal^{19,23} and masseter areas²⁰ as well as the submandibular triangle were other pain sites mentioned by the patients.²³

Pain Characteristics

Pain intensity was severe in 5 patients. In 2 patients, including the present case, the pain started out as mild but gradually increased, became severe, and changed from intermittent to continuous.²³ Pain was continuous in 4 patients and intermittent in 2 patients.¹⁹ Two patients,²³ including the present case, described the pain as dull and aching; 2 described their pain as sharp, and 1 patient²⁴ described it as pulsating, mimicking neurovascular pain. Pain was aggravated by jaw function in 3 patients,^{20,23} including the present case. Description of pain was completely missing in 2 cases^{18,21} and partially missing in another 2 cases.^{9,20}

Asymmetry of the Soft Palate

Examination of the soft palate was mentioned in 2 cases.^{21,24} Asymmetry of the soft palate was observed in only 1 patient.²¹

Neurologic Findings

Four patients^{19,20,23,24} had sensory impairment of the trigeminal nerve. In 2 of the 4 patients,^{20,23} this impairment developed at a later stage. In 1 patient,¹⁹ the pain had characteristics similar to those of a trigeminal neuralgia; however, trigeminal neuralgia was not confirmed by the neurologist. In 3 cases,^{19,20,22} although the patient was seen by a neurologist, no neurological findings were reported. Two patients were referred to a neurologist prior to final diagnosis.^{23,24} In regard to the other patients, no neurologic consultation was mentioned.

Examination of Masticatory Muscles

Muscle palpation was included in 5 patient reports. The ipsilateral temporalis and masseter were mildly tender to palpation in 3 patients,^{23,24} including the present case. In 1 patient,²⁰ the lateral pterygoids, the masseters, and the left sternocleidomastoid muscle were sensitive to palpation. One patient²² demonstrated only temporalis sensitivity. Administration of local anesthetic to the pterygoid muscles eliminated 75% to 100% of the pain in 2 patients.^{23,24}

Comorbid Findings

Imaging showed degenerative changes of the TMJ of the affected side in 2 patients.^{22,24} There was a history of bilateral mandibular fracture and dental extraction in 1 patient,²¹ and a history of trauma that preceded the symptoms in another.²³

Imaging

CT images showed tumor infiltration with the pterygoid muscles in 4 patients.^{18,19,21,22} However, in 2 patients,²² including the present case, the tumor was not visible in the CT scans taken in the early stage. The infiltration of the pterygoid muscles by the tumor was visible in the MRI scans taken for the present patient (Figs 1 and 2). In the other 4 patients, no imaging was mentioned.

Cervical Lymph Nodes

A small superior deep jugular lymph node was palpated as part of the examination in the present case. In 3 other patients,^{10,20,21} the neck mass appeared at a later stage.

Additional Signs and Symptoms

Additional signs and symptoms included epistaxis,¹⁸ unexplained weight loss,¹⁹⁻²¹ nasal congestion,^{9,19,20} and eye dryness.²⁴

Discussion

As the literature review and the present case have shown, NPC patients have several signs and symptoms also commonly found in TMD patients. These clinical features may therefore erroneously lead to a TMD diagnosis when in fact the patient suffers from an NPC. The following will discuss these signs and symptoms and partially outline

their pathophysiology in order to help the practitioner with the process of forming a differential diagnosis. Furthermore, some differences between these features and those originally reported by Trotter¹⁷ are noted.

Age and Gender

When TMJ pain is present in an adolescent male patient, and especially a preadolescent male patient, the practitioner should always question whether a TMD is the cause of the chief complaint, as an NPC can occur at a young age in high-risk populations.

Pain Characteristics

Approximately 50% of NPC patients present with pain at diagnosis.²⁶ Epstein and Jones⁹ reviewed 52 records of NPC patients for symptoms similar to a TMD. Before treatment, pain was described as aching in 37.5% of the patients, dull in 16.7%, pressing in 12.5%, sharp in 8.3%, throbbing in 4.2%, intermittent in 12.5%, and constant in 8.3%. They concluded that the pain characteristics observed in cases of NPC are for the most part similar to those seen in TMD patients. Huang et al²⁶ described pain characteristics of NPC patients before treatment. Pain intensity was rated low (1 or 2) on a visual analog scale. Only 8% of the NPC patients reported severe pain. Sixty percent had no pain, 22% experienced mild pain, and 10% had moderate pain intensity. Using the McGill Pain Questionnaire, patients never described their pain as stabbing, gnawing, splitting, cramping, sickening, or fearful. The most commonly used pain description was “throbbing,” followed by “intermittent,” “brief,” and “continuous.” The last descriptor became more dominant as treatment progressed. Roistacher and Tanenbaum²⁰ and Trumpy and Lyberg²² noted that continuous pain should prompt rethinking regarding a TMD diagnosis, since TMD-related pain is not continuous in nature. It seems that pain characteristics change as the tumor progresses. Pain shifts from mild to severe, becomes continuous, and finally becomes a neuralgic type of pain.¹¹

Comorbid Findings

NPC pain can be located in the preauricular area^{20,22,23} (as in the present case). Therefore, intra-articular findings, such as joint noises and TMJ degenerative changes (as seen on imaging)

could lead to a false diagnosis of an arthrogenous pain.²⁴ The use of analgesic blocks as a diagnostic tool is of paramount importance for a correct diagnosis.^{19,23,24}

Severe Limitation of Mouth Opening

This is often the main reason for suspecting a TMD. However, it is important during the diagnostic process to keep in mind that a limited mouth opening and an opening hard-end limitation have several possible causes, 1 of which is an NPC. It is reasonable to assume that the severely limited mouth opening observed in most of the NPC patients resulted from infiltration of the pterygoid muscles by the tumor, causing interference in the normal function of these muscles. Also of particular interest is the clinical finding that the limited mouth opening was accompanied by a deviation toward the contralateral side in the present case, an observation also reported in another case.²³ Okeson²³ attributed deviation in opening toward the contralateral side to a myospasm of the ipsilateral medial pterygoid. Denervation atrophy of all masticatory muscles ipsilateral to the NPC has been described in a patient, suggesting an intracranial source.¹² However, these muscles were not in a state of trismus. Thus, whether the severe limitation in opening is caused by myospasm of the medial pterygoid or by something else (eg, denervation atrophy) remains unclear.

Muscle Sensitivity to Palpation

Since pain is aggravated by jaw function in some patients,^{20,23} including the present case, muscle tenderness to palpation could erroneously lead to a diagnosis of musculoskeletal pain. Thus, care should be taken not to diagnose a myofascial pain based on muscle tenderness to palpation. Practitioners must recognize that this can also be a manifestation of a central excitatory effect, such as secondary hyperalgesia due to a deep somatic source.^{20,27}

Ear Symptoms

Roistacher and Tanenbaum²⁰ pointed out that ear symptoms associated with TMD are intermittent in nature, as reported by Travell and Simons.²⁸ Therefore, the presence of continuous ear symptoms should lead one to suspect a non-TMD cause, and prompt further examination, especially when they are unrelated to masticatory function. This emphasizes the necessity of an exact description of ear symptoms by the patient.

Asymmetry of Soft Palate

Asymmetry of the soft palate was not examined in most cases. Trotter¹⁷ contended that the reason for palatal asymmetry is not paralysis of the levator palati muscle, but its inability to relax during rest because of tumor infiltration of the muscle. Su et al²⁹ studied the electromyogram (EMG) of the tensor and levator veli palatini muscles in patients with NPC. The abnormal EMG recordings strongly suggested a neurogenic muscle abnormality caused by tumor infiltration of the muscle. Su and Lui³⁰ found ipsilateral paralysis of the palate in 137 (52%) of 264 NPC patients and demonstrated that the degree of paralysis of the levator palati muscle correlated with the degree of invasion of the levator muscle by the tumor as seen in MRI scans. They concluded that this subtle sign is relatively common in patients with NPC and should therefore be routinely checked when NPC is suspected.

Neurologic Findings

Su and Lui¹³ studied 110 NPC patients to evaluate the extent of trigeminal perineural tumor invasion and to correlate the findings with neurologic symptoms. They concluded that the neurologic signs are caused by the intracranial spreading of the tumor, as they appear at a later stage of the disease. Indeed, no NPC patient had neurologic signs or symptoms at the early stage of the disease. The pain characteristics and neurologic findings refute the neuralgic type of pain in Trotter's triad, and point to a deep somatic pain with central excitatory effects.

Imaging

CT may fail to show the tumor at an early stage. Since the primary tumor may be small and infiltrating, the loss of muscle borders and obliteration of fat planes are important diagnostic findings that should be evaluated with MRI, including gadolinium diethyltriaminepentaacetic acid (Gd-DTPA) with fat suppression.^{31,32} Therefore, when NPC is suspected, especially at earlier stages, MRI is the imaging technique of first choice.

Cervical Lymph Nodes

The most common sign leading to a diagnosis of NPC is enlargement of cervical lymph nodes.¹⁵ Approximately 49% of patients present this as their primary symptom, which indicates the difficulty of diagnosing this malignancy early. Palpation of cervical and submandibular lymph nodes must therefore be included in the routine examination of any orofacial pain patient.

Conclusions and TMD Implications

A patient with NPC can present with symptoms that mimic TMD. Because of the subtlety of the early signs and symptoms, it is difficult to diagnose NPC in early stages without being familiar with Trotter's syndrome. A revised Trotter's syndrome is proposed to aid the early diagnosis of this malignancy: (a) *continuous* ear symptoms, such as decreased hearing, fullness, and tinnitus; (b) asymmetry of the soft palate; (c) deep somatic pain with central excitatory effects; and (d) a severe hard-end limitation in mouth opening at a later stage.

When a patient is referred to a TMD clinic, the RDC/TMD diagnostic criteria²⁵ may be used to reach a clinical diagnosis. In the present patient, none of the Axis I diagnoses could be applied, which demonstrated the clinical validity of the RDC/TMD in detecting a non-TMD patient in this particular case. However, better definition of the exclusion criteria is important, especially regarding conditions that are not included in the diagnostic criteria but that could mimic TMD (eg, tenderness to palpation of the masticatory muscles, limited mouth opening). Muscle tenderness to palpation has several causes, such as protective cocontraction, delayed-onset muscle soreness, myositis, and myofascial pain with trigger points originating from the cervical area. It can also be due to a widespread muscle disorder such as fibromyalgia or to a manifestation of RDC/TMD Axis II etiology such as a somatoform pain disorder. Finally, it can also be a manifestation of heterotopic pain such as secondary hyperalgesia caused by a deep source, as in the present patient. Therefore, future research should focus on defining the different exclusion criteria for the RDC/TMD in detail. Otherwise, severe consequences and conflicting research results could emerge, limiting our further understanding of the pathophysiological basis of TMD.

Acknowledgments

Without the sophisticated imaging techniques available today, Dr Wilfred Trotter managed to characterize the NPC patient profile in the early stages of the disease based on a superb diagnostic approach, as well as on the signs and symptoms of only 14 patients. This review is dedicated to Dr Trotter, a young assistant surgeon to be remembered and from whom we can learn, and to the patient whose case was presented here.

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