



Octreotide as a new option for the management of chylous fistula after neck dissection

Nova možnost konzervativnega zdravljenja hilozne fistule po disekciji na vratu z oktreotidom

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Abstract

One of the complications of neck dissection is chylous fistula. Usually, it is a consequence of a thoracic duct injury. A swelling forms in the lower neck area on the left side. Clear or milky-white fluid discharge can be seen. The colour of the fluid depends on the fat content. The goal of the treatment is closure of the fistula and a complete stop of the leak. Conservative methods consist of nutritional support, such as low-fat diet, diet with medium-chain triglycerides, fat-free diet, pressure dressings, and novel management with octreotide. It inhibits the production of chyle, thus enabling the fistula to heal.

Two patients with chylous fistula are reported, who were successfully treated with conventional conservative methods and octreotide. A literature review was conducted on the use of octreotide for the management of chylous fistula following neck dissection.

Octreotide in combination with conventional conservative methods successfully closes the majority of chylous fistulas on the neck without revision surgery.

Izveček

Eden od zapletov disekcije na vratu je hilozna fistula. Največkrat nastane zaradi poškodbe torakalnega voda. Vidi se oteklina nizko na vratu levo. Iz rane lahko izteka tekočina, ki je prozorna ali mlečne barve, kar je odvisno od vsebnosti maščob. Cilj zdravljenja je popolno prenehanje izcejanja tekočine. Od konzervativnih metod se najpogosteje uporablja prehrana z manj maščobami, s srednje dolgimi trigliceridi, brez maščob, kompresijsko povijanje in v zadnjem času oktreotid, ker zavira tvorbo hilozne tekočine. Zato se fistula lažje zaceli.

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Opisujemo dva bolnika s hillozno fistulo na vratu, pri katerih smo ob konzervativnih ukrepih uspešno uporabili oktreotid. Iz literature smo povzeli podatke o zdravljenju hilloznih fistul po disekciji na vratu z oktreotidom.

Zdravljenje z oktreotidom v kombinaciji z že ustaljenimi konzervativnimi postopki zapre večino hilloznih fistul na vratu brez kirurške revizije.

1 Introduction

Chylous fluid or chyle is a lymph fluid that contains vitamins, proteins, lymphocytes, immunoglobulins, electrolytes, and fats. From the small intestine, where it forms, it flows to the thoracic duct (*lat. ductus thoracicus*) and then into the large veins in the neck (1).

Chylous fistula (CF) is a pathological leakage of the chyle from the lymphatic vessel (2). The causes of CF, its location and treatment options are diverse. This article discusses CF in the neck (NCF), which occurs as a complication of cervical lymph node dissection, and a recent treatment option with octreotide (OCT).

1.1 Anatomy of the lymphatic system

Lymphatic vessels have a fragile, thin and transparent wall. The thoracic duct, which collects lymph from the left half of the thorax, begins in the abdominal cavity at the level of the second lumbar vertebra with the chyle cistern (*lat. cisterna chyli*). Lymph flows into it from the abdominal cavity, pelvis and lower limbs (3) – Figure 1.

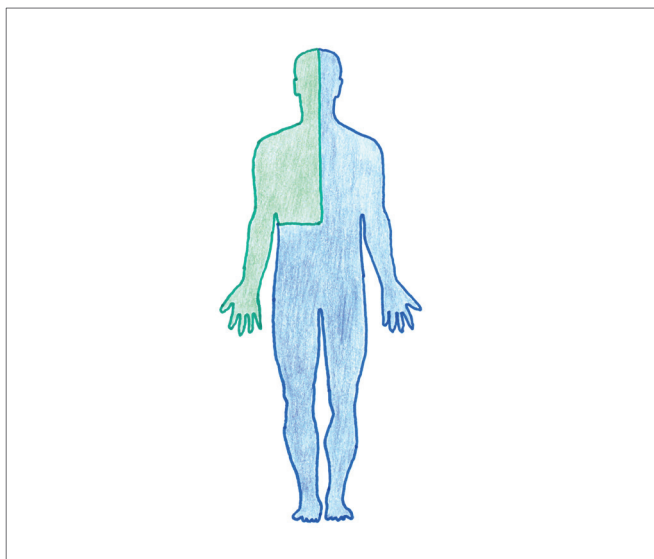


Figure 1: The drainage area of the thoracic duct is shown in blue and the right lymphatic duct in green. Taken from Gilroy MA, Atlas of Anatomy, 2009 (4).

In the neck, the thoracic duct runs upward along the medial edge of the left scalenus medius muscle (2). At the level of the 7th cervical vertebra, it turns forward and downward in an arc and joins the junction of the left subclavian and left jugular veins (*lat. angulus venosus*) (5). The arc of the duct reaches a height of 0.5–4 cm above the clavicle before joining the venous system as one or more canals (6) (2) – Figure 2.

The left subclavian duct (*lat. truncus subclavius sinister*), which collects lymph from the left upper limb, and the left jugular duct (*lat. truncus jugularis sinister*), which collects lymph from the left half of the neck and head, flow into the cervical part of the thoracic duct. The right lymphatic duct (*lat. ductus lymphaticus dexter*) is only a few centimetres long and flows into the venous angulus on the right. It collects lymph from the right upper limb, the right half of the chest, and the right half of the head and neck (3) – Figure 1.

Lymph flow in the thoracic duct amounts to 2–4 l/day and is mostly dependent on diet and also on peristalsis, coughing, breathing, and movement (8).

1.2 Causes and incidence of chylous fistula in the neck

NCF occurs due to diseases of the lymphatic system, malignant diseases, injuries, and most often after operations (2), when it occurs due to rupture of the thoracic duct (2,9). There was also a case of spontaneous occurrence of NCF recently described in the literature (10).

The incidence of NCF after dissection is 0.62–6.2% (11). Due to the course of the thoracic duct, NCF is more common on the left side, but right-sided fistulae are reported in as many as 20–33% of cases (12–14). The incidence is higher if the dissection is bilateral or radical, if the metastases are low in region IV (11) and after irradiation (5).

The consequences of NCF are serious and even life-threatening, so timely identification and rapid action are crucial to improve the outcome (11).

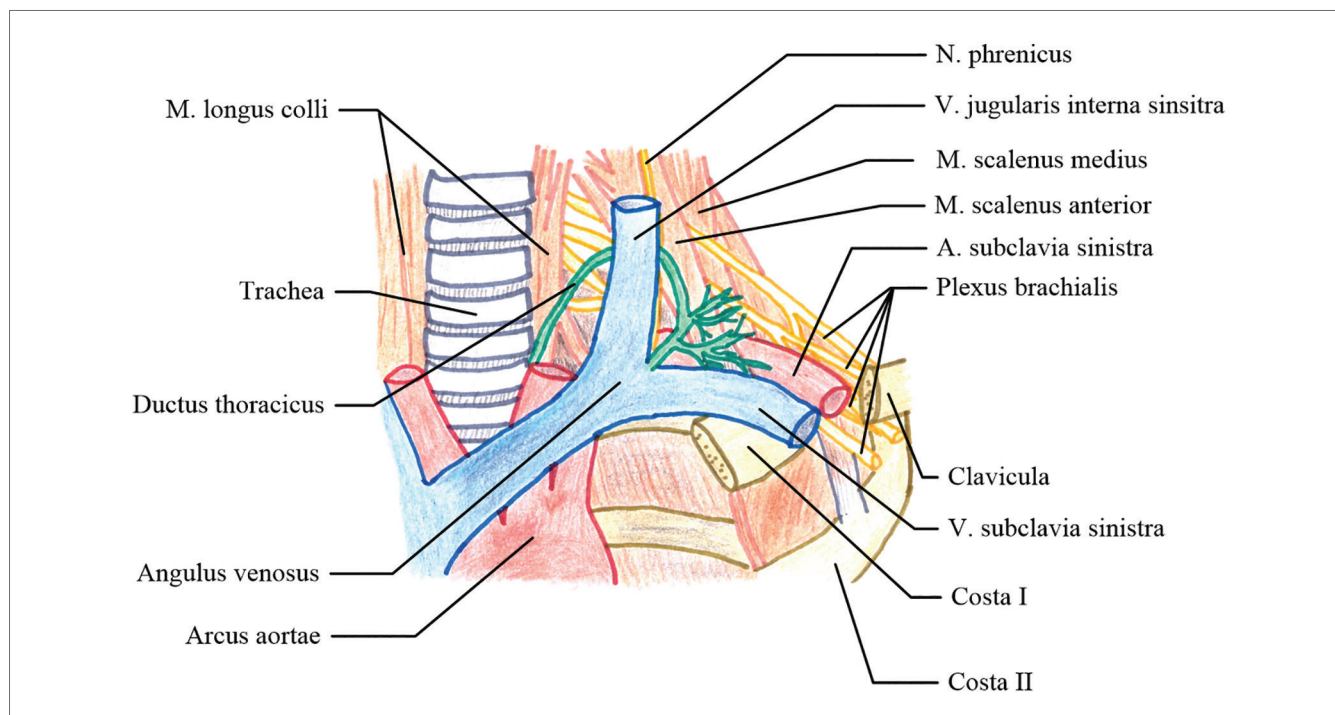


Figure 2: Anatomy of the thoracic duct in the neck. Taken from Gilroy MA, Atlas of Anatomy, 2009 (7).

Legend: N – nervus, V – vena, M – musculus.

1.3 Diagnosis, clinical picture and consequences

The diagnosis of NCF is made clinically (12). Symptoms appear after feeding (2) – a sudden increase in the amount of fluid, a change in the appearance of the fluid and left-sided swelling in the supraclavicular fossa with indurated, red and oedematous skin (14) or fluctuation. The fluid is colourless if the patient does not eat fatty foods, otherwise it becomes milky white (2). According to the output limit of 1 l/day, NCF is divided into fistulae with high and low output (6,9,11,12).

In doubtful cases, the patient is burdened with a fatty meal. If it is CF, more fluid will be excreted and it will become cloudy and milky (11,15). In the laboratory, triglycerides (more than 110 mg/dl), proteins (more than 3 g/dl) (2,5) and chylomicrons can be detected in the liquid (5).

CFs are problematic due to fluid and electrolyte loss, leading to electrolyte imbalance (hypochloraemia, hyponatraemia), hypovolaemia, oedema, lack of essential nutrients, lymphocyte loss, weakened immunity, infection, sepsis, and even shock (5,12). They slow the healing of the surgical wound and cause wound dehiscence, necrosis, and salivary fistula (6) as well as failure of reconstructions (14). Finally, they also extend the duration of hospitalization (9).

1.4 Treatment

The goal of treatment is to close the NCF and stop the leakage of chylous fluid. Type of treatment depends on the cause, the amount of secretion, and the location of the fistula (2). The treatment is divided into conservative and surgical. There are no guidelines for treatment yet (11).

Iatrogenic chylous fistula in the neck that was formed and detected during surgery should be resolved immediately by ligation or suturing of the damaged lymph vessel with possible use of tissue adhesives and conservative measures (16). *Conservative treatment* is appropriate for late onset fistulas with low output. The purpose is to reduce the leakage of chylous fluid through the fistula. Measures include dietary restrictions, pressure dressings, vacuum-assisted closure (VAC), drainage, regular aspiration, and rest (9,12,17). The purpose of *surgical treatment* is to close the thoracic duct (by embolization, ligation, interventional lymphangiography, local flaps) or to restore lymph flow into the veins (using microsurgical techniques) (11).

A newer approach is treatment with OCT. It is an analogue of somatostatin – a growth hormone inhibitor. It inhibits the secretion of pancreatic, gastric and intestinal juices and reduces venous pressure in the liver and blood flow in the gastrointestinal tract. It slows

down the formation of chylous fluid in the gastrointestinal tract, thus reducing leakage through the fistula (9,11,12).

2 Case presentation

At the Department of Otorhinolaryngology and Cervicofacial Surgery, University Medical Centre Ljubljana, two patients with NCF after neck dissection were treated with OCT and conservative measures.

2.1 Clinical case 1

A 91-year-old patient underwent surgery for metastases of unknown origin on the left side of the neck. There was a 7 cm large, hard, poorly movable swelling that was located in regions II and III at the time of clinical examination. We performed a modified radical neck dissection of Type I on the left side and a left tonsillectomy. Pathohistological findings showed metastases of poorly differentiated glandular carcinoma in 25 of the 30 lymph nodes removed by perineural, vascular, and lymphatic invasion. The metastases were located in all five regions, including below the clavicle. Later, the patient was treated with adjuvant radiation.

The patient began with oral feeding the first day after surgery. On the eleventh day, we observed a swelling on the left side of the neck and the patient was bandaged with pressure dressings. On the thirteenth day, we introduced a protein dietary supplement. The day after, serous-milky fluid leaked from the surgical wound above the left clavicle. NCF was diagnosed. The passive drain and wound compression were introduced and a low-fat hypolipaeamic diet (LFD) was started. As there was no improvement, we prescribed OCT, 0.1 mg every 8 hours, subcutaneously, on the 16th day after surgery. The amount of discharge decreased significantly within 5 days of OCT treatment in combination with other conservative measures (LFD, protein supplements, pressure dressing) and after 7 days (i.e. 23 days after surgery) there was no more discharge. The patient received OCT until the 24th day after surgery, when he was discharged. There were no NCF problems at follow-up.

2.2 Clinical case 2

A 56-year-old patient with bipolar disorder and COPD who had undergone a left upper lung lobectomy for squamous cell carcinoma, was treated for a month-and-a-half-long and increasing dyspnea, a foreign body sensation in the throat, hoarseness, and inspiratory

stridor. Upon admission, we found an extensive tumour of the supraglottis that obstructed the airway and completely covered the glottis, and a 2 cm large lump on the left side of the neck in region II. Because the patient had difficulty breathing, we first performed an emergency tracheostomy under local anaesthesia and then direct laryngoscopy under general anaesthesia. The tumour infiltrated the epiglottis and the left ventricular fold. Histological examination of the tumour sample revealed non-keratinizing squamous cell carcinoma of basaloid morphology.

Laryngectomy with bilateral neck dissection was performed. Apart from poorer visibility of tissues due to fibrosis after tracheostomy and thus more difficult thyroid preparation, there were no specific features or complications during the procedure. Pathohistological examination of the primary tumour revealed non-keratinizing squamous cell carcinoma of basaloid morphology 3 cm in diameter and 12 mm thick with lymphovascular invasion. Analysis of the resected tissue from the right side of the neck in the 26 lymph nodes revealed no metastases, and on the left, one of the 23 lymph nodes was positive with a diameter of 35 mm with no extracapsular extension. The operation was followed by radiation.

The patient was fed by a nasogastric tube the first day after surgery. On the fifth day, copious leakage of serous fluid from the surgical wound on the right of the neck was noted. Pharyngocutaneous fistula was ruled out with the help of Gentiana violet dye that the patient swallowed. On the same day, we began to bandage the patient with pressure dressings and on the sixth day we introduced a fat-free diet (FFD). As there was no improvement, we prescribed OCT, 0.1 mg every 8 hours, on day eleven. It was a high-output NCF. Leakage gradually decreased and completely ceased on day 18 after surgery. The patient received OCT for a total of nine days. He was discharged on the 21st day after surgery. There were no more problems with NCF.

3 Discussion

The anatomical diversity of the thoracic duct, its thin and vulnerable transparent wall and difficult recognition during dissection increase the risk of iatrogenic injury (8,13).

3.1 Treatment with dietary restrictions

Dietary restrictions are the basis of CF treatment (17). The purpose is to reduce the formation of chylous fluid in the gastrointestinal tract and thus leakage

through the fistula in the neck, the need to electrolyte replacements, energy and protein loss. The diet is enteral and it includes LFD, FFD, medium-chain triglycerides (MCT), enteral nutrition with a special formula and total parenteral nutrition or combinations (11).

In the treatment of NCF, a diet with MCT holds great promise. After absorption, medium-chain triglycerides reach the venous system through the portal circulation, but not through the thoracic duct. The flow of chylous fluid in it is therefore reduced, diminishing the load on the fistula. In this way the NCF is allowed to heal (11). At the Department of Otorhinolaryngology and Cervicofacial Surgery of the University Medical Centre Ljubljana, we always start with the addition of protein and depending on the amount of discharge with LFD or FFD. We did the same in the two described cases.

3.2 Treatment with other conservative methods

The pressure of *pressure dressings* reduces the fistula output and thus enables healing (12). We applied this principle to our patients as well. VAC is designed to treat complex, chronic wounds that heal poorly. The use of it in the head and neck area has been described in a small number of studies (11). The wound is covered, sealed, and exposed to a vacuum that evenly sucks excess fluid from the entire area of the wound. *Orlistat* is a pancreatic lipase inhibitor that inhibits the breakdown and absorption of fat in the duodenum and reduces the formation of chylous fluid (5). Tao Wei reports on *injection of dead Pseudomonas aeruginosa bacteria* into the wound. Local inflammation occurs with fibrosis that leads to the closure of the fistula (8).

3.3 Treatment with octreotide

OCT is a somatostatin analogue, which is a peptide with paracrine hormone and neurotransmitter function. It inhibits the thyroid-stimulating hormone, growth hormone, vasoactive intestinal peptide, gastrin, motilin, insulin and glucagon. It reduces the flow of bile and the secretion of juices of the pancreas, stomach and intestines, venous pressure in the liver and blood flow in the gastrointestinal tract. It consequently reduces the formation of chylous fluid and thus its output from NCF (9,11,12). OCT is an already established treatment for chylothorax (5,11,18-21). Regarding the treatment of NCF in the neck, this is a newer approach, described only in individual studies (2,5,9,11,12,17,21). OCT is applied subcutaneously (4) and it works fast. It is used as a compelling

addition to other conservative measures for NCF (9,21).

The incidence of side effects is low. Long-term treatment with OCT carries an increased risk of gallstones (9). Nausea, abdominal pain, diarrhoea, hypothyroidism, hyperglycaemia, musculoskeletal pain, bradycardia, and chest pain have also been reported. In less than 1%, it is associated with anaphylactic shock, bile duct obstruction, stroke, gastrointestinal bleeding, and pulmonary embolism. Caution should be exercised when using OCT in patients with heart disease, especially arrhythmias, and liver disease. Swanson believes that short-term treatment with OCT outweighs the risk of long-term CF and the consequences of other treatments (5).

In our patients, NCF was demonstrated based on clinical signs (12), after surgery, and by excluding pharyngocutaneous fistula, as done by Chan as well. In the first case, on the 11th day after surgery, there was swelling at a typical site low on the neck on the left in region IV and above the clavicle, followed three days later by a discharge of serous fluid. The second patient had profuse discharge of serous fluid on day 5 after surgery. Since it was a laryngectomy, we first thought of its most common complication – pharyngocutaneous fistula, which in our experience develops approximately 13 days after primary laryngectomy in 22.5% (22). The dye test definitively ruled it out. What spoke against pharyngocutaneous fistula and in favour of NCF was the time of onset of discharge in the patient (day 5) and a greater amount of discharge than expected.

In both patients, NCF occurred after neck dissection. In the first patient, a fistula developed above the clavicle to the left and in the second patient it developed to the right in region IV. Although the literature describes a higher incidence of NCF on the left side, the incidence of fistulas after dissections of the neck on the right should not be neglected. According to the reports of Ahn and Erisen, NCF occurs on the right in as many as 31.8–33% of cases (13,14). Notwithstanding reports of high incidence of NCF on the right (12-14), the incidence of NCF on the right side in the other patient was surprising because there were no metastases on this side. It can be assumed that anatomical changes of the thoracic duct could have occurred after the left upper lobectomy. The scars in the chest after the operation could have impeded the flow of lymph in the thoracic duct, so the lymph would have been partially redirected to the right lymphatic duct. Due to the expansion, it would have become more susceptible to injury during dissection.

Because the patient was treated with passive drains

and pressure dressings (12), we were unable to quantify the amount of fluid output. Nevertheless, the second patient had high-output NCF, i.e. more than 1 l/day, as he had to have bandages changed four times a day. Each time there was an abundance of chylous fluid to be removed through the drains and the bandage material was completely soaked with it. The literature does not precisely define the indications for surgical treatment (9,12), but in our clinic, we usually perform a surgical revision after a few days with such extensive draining or ineffectiveness of conservative methods.

High-output fistulae are closed by ligation and suturing of the thoracic duct. If we deem necessary, we encourage their healing with a Tachosil patch, which contains fibrinogen and thrombin on an active surface, and additionally protect them with a sternocleidomastoid flap as described by Albirmawy (23).

In this case, we opted for OCT treatment. It was used as an addition to conservative methods such as LFD, FFD, protein addition, and pressure dressing. In both patients, the NCF closed. The literature cites OCT as a good option for closing low-output NCF, but there are reports of successful closure even at high outputs (11,13). Both Swanson (5) and Chan (12) report that an NCF closed with an output of as much as 2.3 and 1.8 l/day, and among patients with high-output NCF, Ahn achieved closure of NCF by OCT in 75% (11).

In our patients, cessation of leakage was observed after 7 days of OCT treatment, which is a few days longer than reported by Jain (2). However, there are reports of a much faster effect, even within 24 hours (7). Swanson reports successful treatment with a combination of OCT and dietary measures in 12 NCF patients after neck dissection. After just one day, the amount of fluid excreted in all patients decreased significantly, and after an average of 5.4 days, the NCF closed (5).

Because NCF increases morbidity and prolongs

hospitalization, it should be identified and treated as soon as possible. In both patients, we started with standard conservative measures such as protein supplement, LFD, FFD, pressure dressings, and with OCT, 0.1 mg every 8 hours. The serous fluid output gradually subsided and, in both cases, disappeared after 7 days. No side effects attributable to OCT were observed. As reported by Delaney, every surgeon should consider OCT in the treatment of NCF after head and neck surgery (21). Other studies and these two clinical cases also suggest that a combination of appropriate dietary measures and OCT closes most NCF without the need for surgical revision.

4 Conclusion

In the case of NCF, rapid treatment is essential, for which, unfortunately, there are no established guidelines. The literature first suggests conservative treatment, namely dietary restrictions, which are a successful method of treating low-output fistulas. Treatment with OCT in conjunction with other conservative methods is recognised as increasingly important due to its rapid action, rare side effects, and efficacy in high-output NCF. Based on our encouraging initial experience and literature data, we believe that patients with NCF should first be treated with established conservative procedures and the addition of OCT if deemed necessary. According to the literature, it will most likely spare the patient a revision operation, which is of course necessary in the event of a failure of conservative treatment.

Conflict of interest

None declared.

Inform consent of the patient

Patients gave informed consent for the publication of their case.

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