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KOMPRESIVNA PRIRODA RETROSTERNALNE STRUME

Sažetak: Medijastinalne mase vode poreklo od struktura medijastinuma ili organa vrata i mogu predstavljati primarne benigne, maligne tumore i metastaze. U najvećem broju slučajeva otkrivaju se radiološkim snimanjem (na rendgenskom snimku slika proširenog medijastinuma). U diferencijalno dijagnostičkom pristupu od koristi je akronim *the terrible T* (*thymoma, teratoma, terrible lymphoma and thyroid*). Retrosternalna struma svojim kompresivnim efektom može dovesti do promene boje glasa, otežanog govora, kompresije traheje, a moguć je i sindrom gornje šuplje vene sa proširenjem venskog crteža grudnog koša. Pored vizuelizacije, tiroidni hormoni i tumor markeri mogu biti od pomoći prilikom dijagnostičkog procesa. Prikazali smo pacijentkinju kod koje je tokom obroka došlo do zastoja zalogaja, zatim gubitka svesti i asistolije. Zbog povrede grudnog koša koja je nastala tokom reanimacije učinjena je kompjuterizovana tomografija, koja je pokazala nodularnu formaciju u desnom režnju štitaste žlezde, koja se spušta kroz gornju torakalnu aperturu iza sternuma, sa izraženim kompresivnim efektom na traheju. Na osnovu ispitivanja zaključeno je da postoji struma sa retrosternalnom, medijastinalnom propagacijom sa tireotoksikozom, koja je najverovatnije indukovana jodnim kontrastnim sredstvom. Kod pacijentkinje je uvedena tireosupresivna terapija, a zatim učinjeno hirurško lečenje retrosternalne strume. Kompjuterizovana tomografija predstavlja najpristupačniji oblik vizualizacije za preoperativnu procenu položaja strume i njenu propagaciju, a hirurgija predstavlja zlatni standard u lečenju simptomatskih retrosternalnih struma.

Uvod: Medijastinalne mase vode poreklo od struktura medijastinuma ili organa vrata i mogu predstavljati primarne benigne, maligne tumore i metastaze. U najvećem broju slučajeva otkrivaju se radiološkim snimanjem (na rendgenskom snimku slika proširenog medijastinuma). U diferencijalno dijagnostičkom pristupu od koristi je akronim *the terrible T* (*thymoma, teratoma, terrible lymphoma and thyroid*). Retrosternalna struma svojim kompresivnim efektom može dovesti do promene boje glasa, otežanog govora, kompresije traheje, a moguć je i sindrom gornje šuplje vene sa proširenjem venskog crteža grudnog koša. Pored vizuelizacije, tiroidni hormoni i tumor markeri mogu biti od pomoći prilikom dijagnostičkog procesa. Prikazali smo pacijentkinju kod koje je tokom obroka došlo do zastoja zalogaja, zatim gubitka svesti i asistolije. Zbog povrede grudnog koša koja je nastala tokom reanimacije učinjena je kompjuterizovana tomografija, koja je pokazala nodularnu formaciju u desnom režnju štitaste žlezde, koja se spušta kroz gornju torakalnu aperturu iza sternuma, sa izraženim kompresivnim efektom na traheju. Na osnovu ispitivanja zaključeno je da postoji struma sa retrosternalnom, medijastinalnom propagacijom sa tireotoksikozom, koja je najverovatnije indukovana jodnim kontrastnim sredstvom. Kod pacijentkinje je uvedena tireosupresivna terapija, a zatim učinjeno hirurško lečenje retrosternalne strume. Kompjuterizovana tomografija predstavlja najpristupačniji oblik vizualizacije za preoperativnu procenu položaja strume i njenu propagaciju, a hirurgija predstavlja zlatni standard u lečenju simptomatskih retrosternalnih struma.

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ćem broju slučajeva otkrivaju se radiološkim snimanjem (na rendgenskom snimku slika proširenog medijastinuma) [1]. U diferencijalno dijagnostičkom pristupu od koristi je akronim *the terrible T* (*thymoma, teratoma, terrible lymphoma and thyroid*). Medijastinalne mase predstavljaju veliki dijagnostički izazov zbog svoje različite etiologije i mogu dovesti do brojnih komplikacija zbog bliskog kontakta sa torakalnim strukturama [2]. Prisustvo određenih kliničkih simptoma, njihova težina i trajanje, kao i prisustvo dodatnih znakova i simptoma mogu biti od pomoći za postavljanje dijagnoze [3]. Multidisciplinarni pristup, koji uključuje saradnju endokrinologa, radiologa, patologa i hirurga, od suštinskog je značaja za postavljanje dijagnoze. To obuhvata patofiziologiju, kliničku prezentaciju, dijagnostiku i lečenje medijastinalnih tumorskih masa [1].

Prikaz slučaja: Pacijentkinja MB, starosti 47 godina, hospitalizovana na Klinici za endokrinologiju, dijabetes i bolesti metabolizma, radi evaluacije retrosternalne strume. Iz anamnestičkih podataka saznajemo da je tokom obroka došlo do zastoja zalogaja, zatim gubitka svesti i asistolije, koja je zahtevala reanimaciju. Zbog povrede grudnog koša, koja je nastala tokom reanimacije, učinjena je kompjuterizovana tomografija, koja je pokazala nodularnu formaciju u desnom režnju štitaste žlezde koja polazi od gornjeg dela desnog lobusa i izlazi kroz gornju torakalnu aperturu iza sternuma, a ispred vaskularnih struktura, veličine 76x57 mm sa izraženim kompresivnim efektom na traheju. Pacijentkinja se žali da je prethodno imala problema sa zadržavanjem hrane, ali nije imala tegobe hipermetabolizma. Inicijalni tiroidni hormonski status je ukazivao na supkliničku hipertireozu, a nakon kontrastnog snimanja, pored nižih vrednosti TSH (0.13... 0.02 mIU/L), registruje se i porast fT4 (21.9... 23.8 pmol/L) – (tabela 1), što je ukazalo na blagu klinički manifestnu hipertireozu, uz uredna tiroid-specifična antitela. Na našoj Klinici na ciljanom CT-u vrata i grudnog koša (slika 1) potvrđena je uvećana štitasta žlezda na račun desnog lobusa, polinodozno izmenjena. U gornjem medijastinumu izdvaja se heterodenzna, delom kalcifikovana postkontrastno opacifikovana promena promera oko 68x77x75 mm. Opisana promena je u bliskom kontaktu sa desnim lobusom štitaste žlezde (u jednom segmentu bez jasno vidljivog masnog plana). Traheja je suženog lumena, potisnuta posteriorno i u levu stranu. Tokom hospitalizacije učinjeno je ispitivanje porekla medijastinalne mase i zaključeno je da se radi o retrosternalnoj strumi veličine 10 cm. Budući da je registrovana tireotoksikoza, koja je najverovatnije indukovana jednim kontrastnim sredstvom, uvedena je tireosupresivna terapija do postizanja eutiroidnog stanja, a zatim je učinjena i totalna tiroidektomija. Postoperativno je uvedena supstitucija levotiroksinom, a histopatološki nalaz je pokazao da se definitivno radilo o retrosternalnoj strumi.

Diskusija: Retrosternalna struma, koja predstavlja uvećanu štitastu žlezdu, može se manifestovati kao medijastinalna masa [3]. Prema svom poreklu, retro-

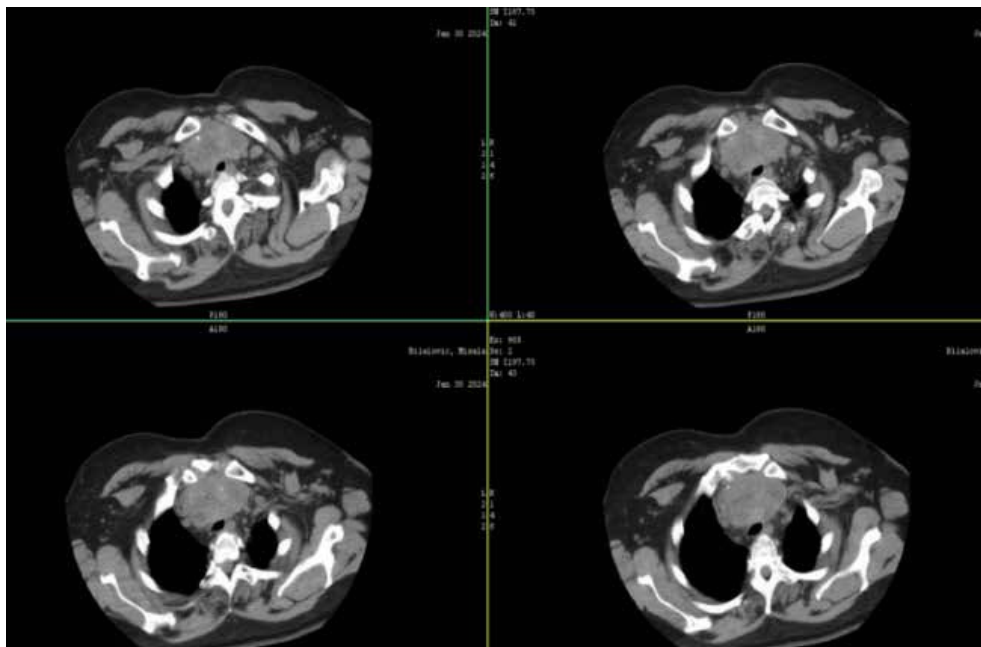
sternalna struma može biti primarna i sekundarna. Primarna retrosternalna struma nastaje od ektopičnog tkiva štitaste žlezde, poreklom od endoderma prednjeg creva, što predstavlja *de novo* retrosternalnu strumu i čini samo 2% svih retrosternalnih struma. Može biti lokalizovana u prednjem ili zadnjem medijastinumu. Sekundarna retrosternalna struma nastaje zbog uvećanja štitaste žlezde, tj. uvećanja jednog ili oba režnja i posledične propagacije kroz torakalnu aperturu. Najčešće je smeštena u prednjem medijastinumu, a ređe u zadnjem medijastinumu [4,5]. Svojim kompresivnim efektom može dovesti do respiratornih simptoma u vidu dispneje, kašlja i osećaja gušenja usled kompresije na traheju. Moguća je i plućna hipoperfuzija, pleuralni izliv, insuficijencija desnog srca, kao i kompresija plućne arterije [6]. Disfagija je čest simptom kod pacijenata sa strumom, koja nastaje zbog kompresije jednjaka između traheje napred i tiroidne mase pozadi [7]. Sindrom gornje šuplje vene sa приметnim proširenjem venskog crteža grudnog koša je česta pojava kod pacijenata sa substernalnom strumom [8, 9]. Kod proširenja venskog crteža grudnog koša potrebno je zamoliti bolesnika da podigne ruke iznad glave, ako se pojavi ili pogorša već postojeće proširenje venskog crteža vrata i facijalna plethora – pozitivan Pembertonov znak – reč je o opstrukciji gornje aperture toraksa [7, 10]. Takođe, može se razviti tranzitorni ishemijski atak, cerebralni edem, paraliza glasnih žica usled kompresije *nervusa laringeusa recurrens*-a, Hornerov sindrom, hilotoraks usled kompresije *ductus thoracicus*-a, perikardni izliv i laringofaringealni refluks [6, 11, 12, 13]. Palpacijom se može utvrditi prisustvo strume i njeni kvaliteti: difuzna ili polinodozna, veličina, konzistencija, pokretljivost, osetljivost, odnos prema koži i strukturama na kojima leži (traheja). Kod pacijenata sa strumom potrebno je uraditi funkcionalno ispitivanje štitaste žlezde kako bi se isključili hipotiroidizam i tireotoksikoza [8, 9]. Potrebno je pratiti vrednosti TSH i fT4, a vrednosti kalcitonina u slučajevima sa sumnjom na medularni karcinom [14, 15]. Nalaz koji bi upućivao na hipo- ili hipertireozu zahteva dalje ispitivanje, a ukoliko je struma difuzna, umerene veličine i bez poremećaja funkcije, dalja ispitivanja i lečenje nisu potrebna [8, 9]. Ultrazvučna dijagnostika je jedna od metoda snimanja koja se često koristi za određivanje zapremine i strukture tiroidnog tkiva, veličine, oblika i sastava čvorova i mogućih metastatskih limfnih čvorova [16]. Rendgenski snimak grudnog koša može pokazati masu gornjeg medijastinuma, devijaciju ili kompresiju traheje. Pacijentima sa znacima i simptomima opstrukcije, kao što su otežano gutanje, kompresija traheje i plethora, treba uraditi vizuelizacionu dijagnostiku, kao što su CT ili NMR, koje pomažu u proceni retrosternalne propagacije strume ili infiltracije okolnih struktura vrata i gornjeg medijastinuma. Treba napomenuti da primena jodnih kontrastnih sredstava može da izazove razvoj tireotoksikoze [8, 9]. Scintigrafija štitaste žlezde se danas znatno manje koristi nego ranije, korisna je ukoliko postoji nodozna struma sa niskim TSH kako bi se ocenila funkcijska aktivnost nodusa ili kod sumnje na tiroidnu ektopiju i retrosternalnu

propagaciju. Punkcija tankom iglom je najpouzdaniji postupak za ocenu biološke prirode nodozne strume. Rezultat citopatološkog pregleda punktata može da bude benigni, maligni, lažno pozitivan, lažno negativan i neadekvatan uzorak. Postupak ne može da napravi razliku između folikularnog karcinoma i benignog folikularnog adenoma, kada je potreban histopatološki pregled uzorka dobijenog operacijom. Histopatološki nalazi kod retrosternalne strume najčešće upućuju na papilarni karcinom (72,4%), folikularni karcinom (26,8%) i medularni karcinom (0,8%) [17]. Zbog otežanog pristupa retrosternalnoj regiji mogu nastati povrede intratorakalnih vaskularnih struktura i okolnih struktura, stoga se punkcija retko izvodi kod pacijenata sa retrosternalnom strumom [18]. Kod pacijenata bez simptoma neophodno je praćenje ukoliko dođe do promene u veličini strume, kompresije traheje i promene u funkciji štitaste žlezde, a CT grudnog koša se savetuje jednom godišnje. Ukoliko pacijenti imaju simptome, tj. primećuje se rast substernalne strume, promena boje glasa ili otežanog govora, sindrom gornje šuplje vene sa приметnim proširenjem venskog crteža grudnog koša u obzir dolazi operativno lečenje [19].

Zaključak: Na osnovu anamneznih podataka o srčanom zastoju moguće je da je kod naše pacijentkinje sa velikom retrosternalnom strumom došlo do gubitka svesti i iznenadnog srčanog zastoja kao posledice vazovagalnog refleksa usled opstrukcije larinksa i traheje stranim telom ili zbog stranog tela zaglavljeno u cervikalnom delu jednjaka. U većini slučajeva, lečenje substernalne strume uključuje hiruršku resekciju da bi se ublažili simptomi, sprečile komplikacije i potvrdila dijagnoza. Kompjuterizovana tomografija predstavlja najpristupačniji oblik vizualizacije za preoperativnu procenu položaja strume, njenu propagaciju i planiranje hirurškog pristupa, a hirurgija predstavlja zlatni standard u lečenju simptomatskih retrosternalnih struma. Hirurgija obuhvata tiroidektomiju sa uklanjanjem retrosternalne komponente, što često, pored cervikalnog reza, zahteva i srednju sternotomiju ili torakotomiju. Postoperativno je neophodna supstituciona terapija levotiroksinom. Moguće su postoperativne komplikacije, kao što su postoperativno krvarenje, povrede *nervus laryngeus recurrens*-a i hipoparatiroidizam. Multidisciplinarni pristup koji obuhvata saradnju između hirurga, onkologa, radiologa i drugih specijalista je od suštinskog značaja za adekvatan ishod lečenja i pružanje sveobuhvatne nege prilagođene potrebama pacijenata [1].

Tabela 1. Vrednosti pre operacije

TSH	0.13...0.02...0.02 mIU/L
fT3	6 pmol/L
fT4	21.9...23.8...21 pmol/L
T3	1.93 nmol/L
T4	157 nmol/L
CT	4.8 ng/L
TPOAt	14 IU/mL
TgAt	10 IU/mL
TRAb	0.9 IU/L
PTH	57 ng/L
Vit D	13 nmol/L
Ca	2.46 mmol/L
PO₄	1.17 mmol/L

Slika 1. CT vrata i grudnog koša

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COMPRESSIVE EFFECT OF RETROSTERNAL GOITER

Abstract: Mediastinal masses originate from the structures of the mediastinum or neck organs and can represent primary benign or malignant tumors, as well as metastases. In most cases, they are detected through radiological imaging, such as an X-ray of the enlarged mediastinum. In the differential diagnostic approach, the acronym “the terrible T” (thymoma, teratoma, terrible lymphoma, and thyroid) is useful. A retrosternal goiter with its compressive effect can lead to changes in the voice, difficult speaking, tracheal compression, and potentially superior vena cava syndrome. Additionally, visualization techniques, thyroid hormones, and tumor markers can be helpful in the diagnostic process. We presented a patient who, during a meal, stopped eating, lost consciousness, and experienced asystole. Due to a chest injury sustained during resuscitation, a computerized tomography (CT) scan was performed. The CT scan revealed a nodular formation in the right lobe of the thyroid gland that extends through the upper thoracic aperture behind the sternum, exerting a pronounced compressive effect on the trachea. Based on the examination, it was concluded that the patient has a goiter with retrosternal and mediastinal extension, accompanied by thyrotoxicosis, which was most likely induced by the iodine contrast agent. Thyrostatic therapy was initiated, followed by surgical treatment of the retrosternal goiter. Computed tomography is the most accessible form of imaging for preoperative assessment of goiter position and its extent, while surgery remains the gold standard for treating symptomatic retrosternal goiters.

Introduction: Mediastinal masses originate from structures within the mediastinum or neck organs and can include primary benign or malignant tumors, as well as metastases. They are typically detected through radiological imaging, such as X-ray images of the enlarged mediastinum [1]. In differential diagnosis,

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the acronym “the terrible T” (thymoma, teratoma, terrible lymphoma, and thyroid) is useful. Mediastinal masses pose a significant diagnostic challenge due to their varied etiology and potential complications from their close proximity to thoracic structures [2]. The presence, severity, and duration of certain clinical symptoms, along with additional signs, can aid in establishing an accurate diagnosis [3]. A multidisciplinary approach involving endocrinologists, radiologists, pathologists, and surgeons is essential for establishing a diagnosis. This approach encompasses the pathophysiology, clinical presentation, diagnosis, and treatment of mediastinal tumor masses [1].

Case Report: Patient MB, a 47-year-old, was hospitalized at the Clinic for Endocrinology, Diabetes, and Metabolic Diseases for evaluation of a retrosternal goiter. From the anamnesis, it is noted that during a meal, the patient experienced a pause in eating, followed by loss of consciousness and asystole, which required resuscitation. Due to a chest injury sustained during resuscitation, a computerized tomography (CT) scan was performed. The CT scan revealed a nodular formation in the right lobe of the thyroid gland, extending from the upper part of the lobe and protruding through the upper thoracic aperture behind the sternum and in front of the vascular structures. The nodule measures 76x57 mm and exerts a pronounced compressive effect on the trachea. The patient reports a history of difficult with food retention but denies symptoms of hypermetabolism. The initial thyroid hormone status indicated subclinical hyperthyroidism. After contrast imaging, in addition to lower TSH values (0.13... 0.02 mIU/L), an increase in fT4 levels (21.9... 23.8 pmol/L) – (table 1) was noted, which suggested mild clinically manifest hyperthyroidism with normal thyroid-specific antibodies. At our Clinic, a targeted CT scan of the neck and chest (figure 1) confirmed an enlarged thyroid gland, predominantly affecting the right lobe, with evidence of polynodosis. In the upper mediastinum, a heterodense, partially calcified, post-contrast opacified lesion with a diameter of approximately 68x77x75 mm was identified. The described mass is in close contact with the right lobe of the thyroid gland, appearing in one segment without a clearly visible fat plane. The trachea exhibits a narrowed lumen, which is pushed posteriorly and to the left. During hospitalization, the origin of the mediastinal mass was investigated, and it was determined to be a retrosternal goiter measuring 10 cm. Given the thyrotoxicosis, likely induced by the iodine contrast agent, thyrostatic therapy was initiated until a euthyroid state was achieved, followed by a total thyroidectomy. Postoperatively, levothyroxine substitution was introduced, and histopathological findings confirmed the diagnosis of a retrosternal goiter.

Discussion: A retrosternal goiter, which represents an enlarged thyroid gland, can be presented as a mediastinal mass [3]. Depending on its origin, a retrosternal

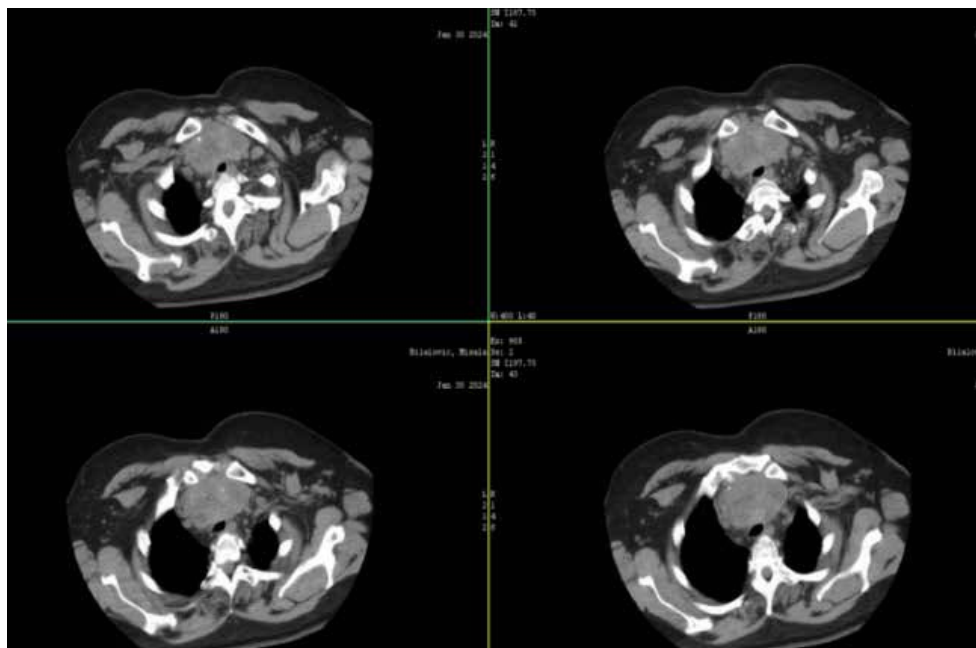
goiter can be classified as either primary or secondary. Primary retrosternal goiter arises from ectopic thyroid tissue, originating from the endoderm of the foregut. This *de novo* retrosternal goiter accounts for only 2% of all retrosternal goiters and can be located in either the anterior or posterior mediastinum. Secondary retrosternal goiter results from the enlargement of the thyroid gland, either of one or both lobes, which then propagates through the thoracic aperture. It is most commonly found in the anterior mediastinum and less frequently in the posterior mediastinum [4,5]. Due to its compressive effect, a retrosternal goiter can cause respiratory symptoms such as dyspnea, cough, and a sensation of suffocation due to tracheal compression. Pulmonary hypoperfusion, pleural effusion, right heart failure, and pulmonary artery compression are also possible [6]. Dysphagia is a common symptom in patients with goiter, caused by compression of the esophagus between the trachea anteriorly and the thyroid mass posteriorly [7]. Superior vena cava syndrome, characterized by noticeable enlargement of the chest's venous pattern, frequently occurs in patients with substernal goiter [8,9]. To evaluate this, ask the patient to raise their arms above their head. If the venous pattern in the neck becomes more prominent or facial plethora develops, indicating a positive Pemberton's sign, this suggests obstruction of the upper thoracic aperture [7,10]. Additionally, complications such as transient ischemic attack, cerebral edema, vocal cord paralysis due to compression of the recurrent laryngeal nerve, Horner's syndrome, chylothorax due to compression of the thoracic duct, pericardial effusion, and laryngopharyngeal reflux may also develop [6,11,12,13]. Palpation can help determine the presence of a goiter and assess its characteristics: whether it is diffuse or nodular, its size, consistency, mobility, sensitivity, and its relationship to surrounding structures such as the trachea. For patients with goiter, a functional examination of the thyroid gland is essential to rule out conditions such as hypothyroidism and thyrotoxicosis [8,9]. Monitoring TSH and fT4 levels is necessary, and calcitonin levels should be checked if medullary thyroid cancer is suspected [14,15]. Findings suggestive of hypo- or hyperthyroidism warrant further investigation. If the goiter is diffuse, of moderate size, and without functional disorders, additional investigations and treatment may not be required [8,9]. Ultrasound is a commonly used imaging method to evaluate the volume and structure of thyroid tissue, the size, shape, and composition of nodules, and any potential metastatic lymph nodes [16]. A chest X-ray may reveal an upper mediastinal mass, tracheal deviation, or compression. Patients exhibiting signs and symptoms of obstruction such as difficulty swallowing, tracheal compression, and facial plethora should undergo imaging studies such as CT or MRI to assess the retrosternal spread of the goiter or infiltration of surrounding structures in the neck and upper mediastinum. It is important to note that iodinated contrast agents can induce thyrotoxicosis [8,9]. Thyroid scintigraphy, although less commonly used today, is still useful for

evaluating the functional activity of nodules in cases of nodular goiter with low TSH or when thyroid ectopy and retrosternal extension are suspected. Fine needle aspiration (FNA) is the most reliable method for assessing the biological nature of a nodular goiter. The cytopathological examination of the aspirate may yield results that are benign, malignant, false positive, false negative, or inadequate. FNA cannot differentiate between follicular carcinoma and benign follicular adenoma; therefore, a histopathological examination of the surgical specimen is necessary for a definitive diagnosis. Histopathological findings in retrosternal goiter most commonly indicate papillary carcinoma (72.4%), follicular carcinoma (26.8%), and medullary carcinoma (0.8%) [17]. Due to the challenging access to the retrosternal region, there is a risk of injury to intrathoracic vascular structures and surrounding tissues, which is why fine needle aspiration (FNA) is rarely performed in patients with retrosternal goiter [18]. For asymptomatic patients, follow-up is important if there are changes in the size of the goiter, tracheal compression, or alterations in thyroid function. A chest CT scan is recommended annually. For symptomatic patients such as those experiencing growth of a substernal goiter, changes in voice, difficulty speaking, or superior vena cava syndrome with noticeable expansion of the chest venous pattern operative treatment is considered [19].

Conclusion: Based on the anamnesis data, it is possible that our patient with a large retrosternal goiter experienced loss of consciousness and sudden cardiac arrest due to a vasovagal reflex triggered by obstruction of the larynx and trachea, possibly from a foreign body or an obstruction in the cervical part of the esophagus. In most cases, the treatment of substernal goiter involves surgical resection to alleviate symptoms, prevent complications, and confirm the diagnosis. Computed tomography (CT) is the most accessible method for preoperative assessment of the goiter's position, its propagation, and planning the surgical approach. Surgery remains the gold standard for treating symptomatic retrosternal goiters. The surgical procedure typically includes thyroidectomy with removal of the retrosternal component, which often requires a median sternotomy or thoracotomy in addition to a cervical incision. Postoperatively, levothyroxine replacement therapy is essential. Potential postoperative complications include bleeding, recurrent laryngeal nerve injury, and hypoparathyroidism. A multidisciplinary approach, involving collaboration among surgeons, oncologists, radiologists, and other specialists, is crucial for achieving optimal treatment outcomes and providing comprehensive care tailored to the needs of the patient [1].

Table 1. Preoperative values

TSH	0.13...0.02...0.02 mIU/L
fT3	6 pmol/L
fT4	21.9...23.8...21 pmol/L
T3	1.93 nmol/L
T4	157 nmol/L
CT	4.8 ng/L
TPOAt	14 IU/mL
TgAt	10 IU/mL
TRAb	0.9 IU/L
PTH	57 ng/L
Vit D	13 nmol/L
Ca	2.46 mmol/L
PO₄	1.17 mmol/L

Figure 1. CT of the Neck and Chest

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