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CASE REPORTS

CASE REPORT

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Imatinib-resistance without BCR/ABL Point Mutation in Chronic Myeloid Leukemia

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ABSTRACT

Chronic myeloid leukemia (CML) is a myeloproliferative bone marrow neoplasm that occurs because of a fusion gene called *BCR-ABL1*. Imatinib - the inhibitor of this fusion geneis the target therapy in CML. But unfortunately, resistance against imatinib occurs in some patients. In September 2019 47-year-old male was diagnosed with CML-chronic phase and intermediate risk group. Imatinib has been prescribed as a first-line treatment. The patient did not achieve a major molecular response (MMR). Next-generation sequencing using a 54 myeloid-targeted gene panel was negative for *ABL1 L248V, G250E, Y253H, E255K, F311L, T315I, F317L, F311I, M351T*, and other point mutations. After Nilotinib patient achieved MMR within two years. Imatinib resistance is impediment during treating CML. In the future, new molecules for BCR-ABL inhibitors, combination therapy, and molecules entering the blood-brain barrier may improve the outcomes of therapy and prevent imatinib resistance in CML.

Keywords: Imatinib-resistance, CML, ABL1 domain mutations

INTRODUCTION

Chronic myeloid leukemia (CML) is a myeloproliferative bone marrow disease. It presents granulocyte proliferation and a potential rise in the blast count of the bone marrow. This neoplasm occurs because of BCR-ABL fusion. Imatinib, the BCR-ABL tyrosine kinase inhibitor, has been successfully used as a first-line treatment for CML during the last 25 years. Unfortunately, imatinib resistance has been described and has been the main topic in CML research. BCR-ABL domain mutations are the main cause of resistance and are detected in the majority of cases [1]. In addition to these mutations, many other factors play a key role in imatinib resistance, such as the biology of malignant cells, genetic background, gene amplifications, and pharmacologic aspects. In this case report, we described a patient who was resistant to imatinib without any imatinib-resistant mutations.

CASE PRESENTATION

A 47-year-old male with complaints of sore throat and rapid weight loss was diagnosed with CML-chronic phase and intermediate risk group in September 2019. Imatinib has been prescribed as a first-line treatment.

At the onset of the disease, blood smear showed leukocytosis (269.18×10^9/L), anemia (9.5 g/dL), and normal platelet count (389×10^9/L). Ultrasound screening revealed splenomegaly + 7 ms. The bone marrow aspirate smears showed 2% blasts, 15% erythroid cells, 23% immature granulocytes, 39% mature granulocytes, 11% mature lymphocytes, 4% immature eosinophils, 3% basophils, 3% mature eosinophils. Trephine biopsy showed hypercellular marrow with sheets of immature cells, elevated megakaryocytes, and reticulin grade I.

Interphase fluorescence *in situ* hybridization showed *BCR-ABL1* translocation in 100% of the cells. The reverse transcription-polymerase chain reaction (RT- PCR) for the *BCR-ABL1* fusion transcript p210 was detected at 56.322% international scale (IS).

In February 2021, he presented with persistent thrombocytopenia and anemia. RT- PCR for the *BCR-ABL1* fusion transcript p210 was detected at 16.359% IS. At the end of the first year, the patient did not achieve a major molecular response (MMR), although next-generation sequencing using a 54 myeloid-targeted gene panel was negative for *ABL1 L248V, G250E, Y253H, E255K, F311L, T315I, F317L, F311I, M351T*, and other point mutations (Figure 1). Nilotinib is prescribed as a second-line treatment. Within a month, he achieved significant clinical and hematological improvement. At the end of the second year, the patient achieved MMR.

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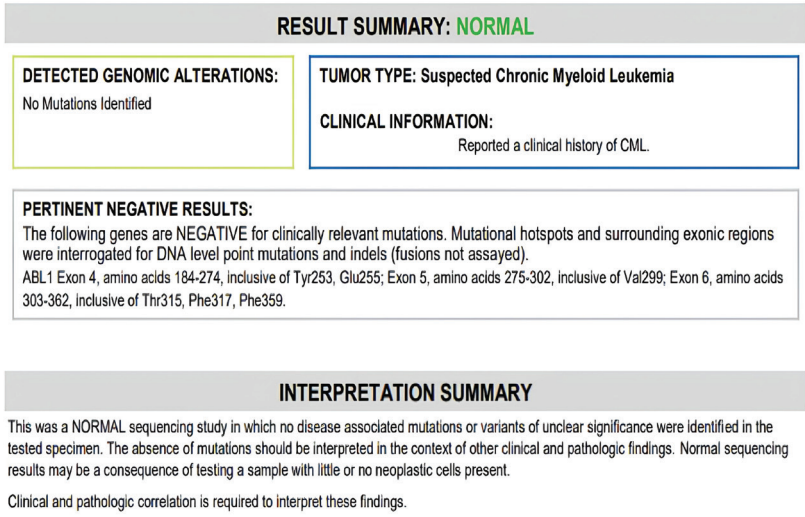

RESULT SUMMARY: NORMAL

DETECTED GENOMIC ALTERATIONS:
No Mutations Identified

TUMOR TYPE: Suspected Chronic Myeloid Leukemia

CLINICAL INFORMATION:
Reported a clinical history of CML.

PERTINENT NEGATIVE RESULTS:
The following genes are NEGATIVE for clinically relevant mutations. Mutational hotspots and surrounding exonic regions were interrogated for DNA level point mutations and indels (fusions not assayed).
ABL1 Exon 4, amino acids 184-274, inclusive of Tyr253, Glu255; Exon 5, amino acids 275-302, inclusive of Val299; Exon 6, amino acids 303-362, inclusive of Thr315, Phe317, Phe359.

INTERPRETATION SUMMARY

This was a NORMAL sequencing study in which no disease associated mutations or variants of unclear significance were identified in the tested specimen. The absence of mutations should be interpreted in the context of other clinical and pathologic findings. Normal sequencing results may be a consequence of testing a sample with little or no neoplastic cells present.

Clinical and pathologic correlation is required to interpret these findings.

Figure 1. The result of the next-generation sequencing using a 54 myeloid-targeted gene panel of the patient
CML: Chronic myeloid leukemia

DISCUSSION

Many patients with chronic phase CML [2] and accelerated phase [3] achieve major cytogenetic and molecular responses with imatinib. However, many patients develop resistance against imatinib, which is often associated with point mutations in BCR-ABL [4]. The prognosis is not favorable for such patients. In addition to molecular resistance against imatinib, other mechanisms such as intrinsic resistance of CML stem cells [5,6], bioavailability of imatinib [7], clonal progression, BCR-ABL-independent signaling pathway involvement, and poor accumulation of imatinib in the central nervous [8,9] have also been described.

Imatinib resistance is a crucial issue in CML treatment. In the future, new, more successful BCR-ABL inhibitors, combination therapy, and molecules that enter the blood-brain barrier may improve the outcomes of CML therapy. This approach can also prevent imatinib resistance in the early phase of CML.

Ethics

Informed Consent: Patient freely and voluntarily gave consent and signed a Informed Consent Form.

Financial Disclosure: The author declared that this study received no financial support.

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CASE REPORT

DOI: 10.4274/cmj.galenos.2024.77486
J Cau Med Sci 2024;2(1):3-4

A Rare Cause of Occult Gastrointestinal Bleeding: Solitary Rectal Ulcer Syndrome

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ABSTRACT

Occult gastrointestinal (GI) bleeding is defined as iron deficiency anemia or positive fecal guaiac test results without obvious bleeding. There are multiple reasons for occult GI bleeding. Despite its rarity, solitary rectal ulcer syndrome (SRUS) can result in occult bleeding. Here we will discuss a case of SRUS.

Keywords: Occult gastrointestinal bleeding, solitary rectal ulcer, dyssynergic defecation

INTRODUCTION

Occult gastrointestinal (GI) bleeding is the presence of a positive fecal occult blood test and/or iron deficiency anemia in the absence of visible blood loss. Common causes of occult GI bleeding include esophagitis, erosive gastritis, peptic ulcer, colon polyps and cancer, inflammatory bowel disease, vascular ectasias, portal hypertensive gastropathy, gastric antral vascular ectasias, and small bowel tumors [1,2]. Although a solitary rectal ulcer usually causes rectal pain and obvious GI bleeding, it can sometimes cause occult GI bleeding [3]. Here we present a patient with solitary rectal ulcer syndrome (SRUS) who presented with occult GI bleeding.

CASE PRESENTATION

A 45-year-old male patient was referred to our clinic with iron deficiency anemia. The patient had no complaints except fatigue. There was no history of melena, hematochezia, or hematemesis. In anamnesis, it was learned that he spent a long time in the toilet, strained a lot, and had the feeling of incomplete evacuation after defecation. These symptoms have existed for a long time. He had no known chronic diseases or medication use. Physical examination did not reveal any pathological findings. Laboratory investigation revealed hemoglobin of 12.4 g/dL, mean corpuscular volume 78, and ferritin 15 mL/ng. The patient underwent upper endoscopy and colonoscopy. Upper endoscopy was normal. Colonoscopy revealed two oval-shaped ulcers, approximately 20 mm in diameter, with white clean base exudate on the second and third Houston valves. SRUS was considered, and biopsies were taken from the ulcer edges to rule out malignancy (Figure 1). The pathology result was reported as a benign ulcer. The patient was administered behavioral therapy. Fiber diet, fluid intake, and topical sucralfate treatment were recommended as first-line treatment.

DISCUSSION

SRUS was first described by Cruveilhier [4] in 1829. The disease has an annual prevalence of 1 in 100,000 people. It occurs most frequently in the third decade in men and in the fourth decade in women, and it can also be seen in young adults. The term SRUS is misnomer because only a quarter of patients have a

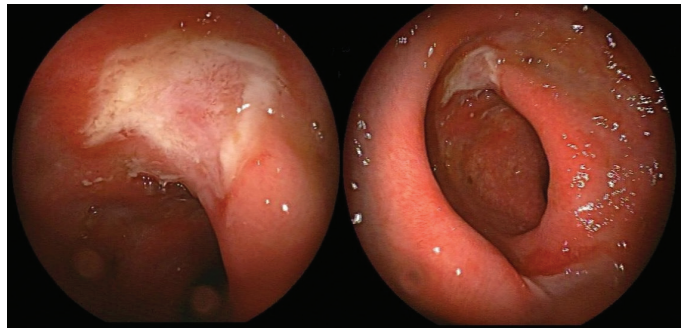

Figure 1. Colonoscopy image shows two white clean base ulcers

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single ulcer. In most cases, multiple ulcers of different shapes and sizes are observed [5]. Two ulcers were present in our patient.

Multiple factors may play a role in the underlying etiology, although it is not fully understood. Direct trauma or local ischemia is the most widely accepted theories. It has been suggested that excessive straining during defecation can lead to trauma and compression of the anterior rectal wall on the upper anal canal, which can cause ischemic damage [6]. Studies have shown that 82% of patients with SRUS may have dyssynergic defecation [7]. Our patient's history was consistent with dyssynergic defecation, which included incomplete evacuation and excessive straining.

Clinical findings of SRUS include rectal bleeding, mucus discharge, and perineal and abdominal pain [8]. The amount of blood varies from small amounts of fresh blood to severe bleeding that requires blood transfusion. However, cases presenting with occult GI bleeding are rare [3]. The diagnosis of SRUS is based on clinical features, rectosigmoidoscopy, and histological examination. A comprehensive history is crucial for SRUS diagnosis. Differential diagnosis includes inflammatory bowel disease, ischemic colitis, and malignancy [9]. It has been reported that the ulcer is usually on the anterior wall of the rectum. The shape and diameter of ulcers can vary but are usually 1-1.5 cm. The ulceration is superficial, and the mucosal membrane surrounding it may be nodular, lumpy, or granular. To exclude other diseases, biopsies should be taken from the ulcer edge and normal or abnormally appearing colon mucosa [3].

The first step for treating SRUS is patient education [10]. In particular, asymptomatic patients may not require any treatment except for behavioral changes. Other suggestions for treatment include encouraging a high-fiber diet, avoiding straining, regulating toilet habits, and improving psychosocial factors. Biofeedback therapy is recommended for patients with dyssynergic defecation who do not respond to treatment [10]. For symptomatic ulcers, topical treatments, including sucralfate, salicylates, corticosteroids, and mesalazine, have been reported to be effective in improving symptoms [11].

In conclusion, patient history is crucial when investigating patients for occult GI bleeding. SRUS should be considered in patients with a history compatible with dyssynergic defecation. Patient education is the initial step in managing SRUS. In symptomatic cases, sucralfate and salicylate treatment can be used.

Ethics

Informed Consent: The patient's written informed consent was obtained.

Authorship Contributions

Surgical and Medical Practices: A.A., Concept: İ.D., Design: A.A., Data Collection or Processing: A.A., Analysis or Interpretation: İ.D., Literature Search: A.A., Writing: A.A.

Conflict of Interest: No conflict of interest was declared by the authors.

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CASE REPORT

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Myocardial Infarction with Non-obstructive Coronary Arteries - MINOCA in Young Patients

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[2]Central Clinic Hospital, Baku, Azerbaijan

ABSTRACT

Myocardial infarction with non-obstructive coronary arteries or MINOCA, is not associated with severe coronary artery stenosis. According to statistics, MINOCA occurs more frequently in women and younger patients. Symptoms and signs are similar to acute myocardial infarction. Coronary artery stenosis was excluded by coronary angiography.

Keywords: Coronary artery spasm, myocardial infarction, atherosclerosis, stenosis, thrombosis, non-obstructive coronary artery disease

INTRODUCTION

MINOCA is a syndrome with features of myocardial infarction but no significant stenosis (i.e., less than 50%) on coronary angiography [1,2]. Rupture of atheroma in the coronary artery due to sudden stress and other reasons, along with platelet adhesion and aggregation, causes thrombus formation. Because it is rich in platelets, it is unstable, and even if it blocks a vessel suddenly, it dissolves within minutes and restores blood flow. Troponin levels can also be elevated because of myocardial damage that occurs when a vessel is completely occluded. Patients with MINOCA tend to be younger and are more common in women. Evidence to date has established that coronary arterial function and disease are not limited to obstructive coronary artery disease (CAD) in women [3].

CASE PRESENTATIONS

CASE 1

A 35-year-old female patient was admitted to the department of cardiology with a complaint of chest pain. On admission, her blood pressure was 210/120 mmHg, heart rate was 75 bpm, and oxygen saturation was 90%. Her past medical history is significant for hyperthyroidism and she has been taking a 10 mg tablet of thirozol regularly for a year. There are no risk factors for CAD.

Blood tests: Hemoglobin: 13.1 mg/dL, white blood count: 6.11 µL, low-density lipoprotein: 242 mg/dL, triglyceride: 164.6 mg/dL, thyroid- stimulating hormone: 4.75 µIU/mL, anti-thyroid peroxidase: 587.2 IU/mL, troponin I: >3.89 ng/mL (Figure 1).

Echocardiography: Left ventricular ejection fraction (LVEF), 35%; lateral and anterior segments are hypokinetic; diastolic dysfunction, grade 1; mild mitral and tricuspid valve regurgitation.

Coronary angiography showed no significant lesions (Figure 2).

Cardiac magnetic resonance imaging (MRI) showed no myocardial damage (Figure 3).

CASE 2

A 28-year-old male patient presented to the emergency department with a 20-minute episode of chest pain. The chest pain was central and radiating to the left arm. Blood pressure was 130/95 mmHg, heart rate was 75 bpm, and oxygen saturation was 97%.

He smoked 20 cigarettes daily but was not aware of any other cardiovascular risk factors.

Complete blood count, normal; troponin I, normal.

Echocardiography: LVEF, 45%, with severe hypokinesis in the mid and basal sections of the anterior segment (Figure 4).

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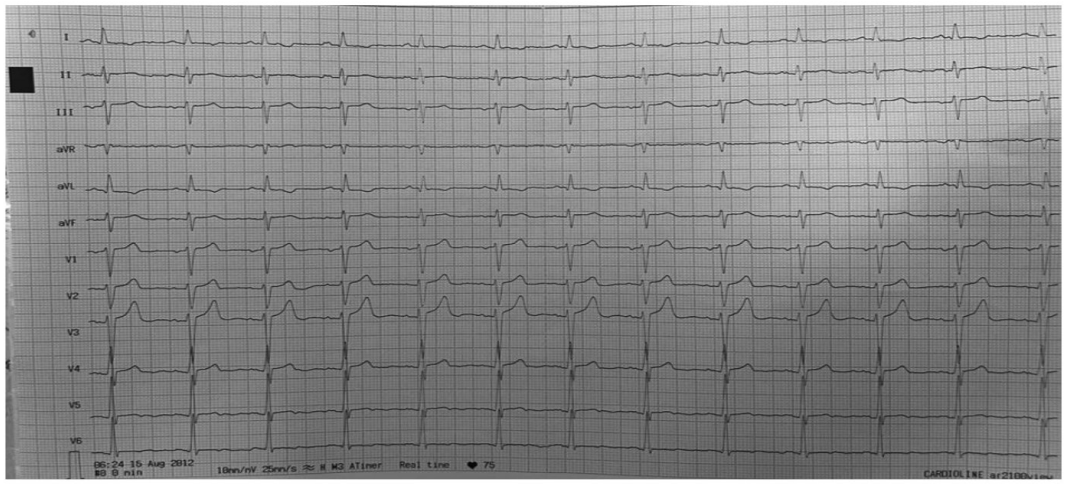

Figure 1. Electrocardiography

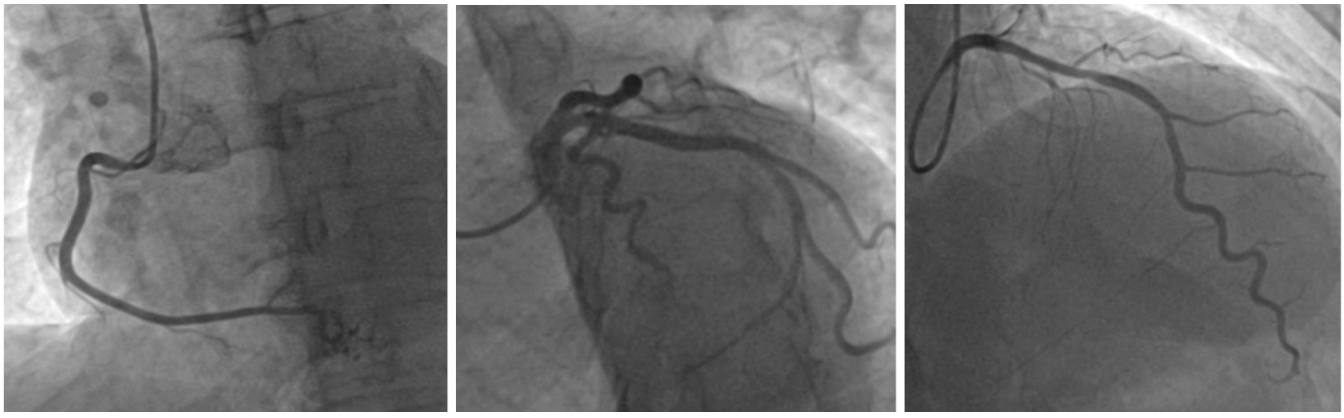

Figure 2. Coronary angiography

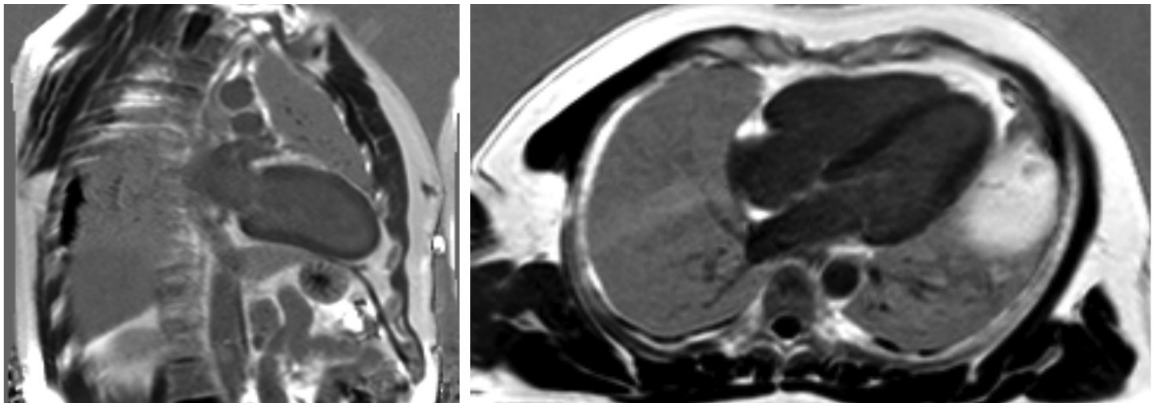

Figure 3. Cardiac MRI
MRI: Magnetic resonance imaging

Cardiac MRI: Observation of ischemic pattern injury, contrast agent retention, and a microvascular obstruction area is noted in the right coronary artery (RCA) region. Considering the angiography results, it was thought that this patient had MINOCA due to transmural damage in the RCA vascular region, despite not having a 100% blocked vessel (Figures 5, 6).

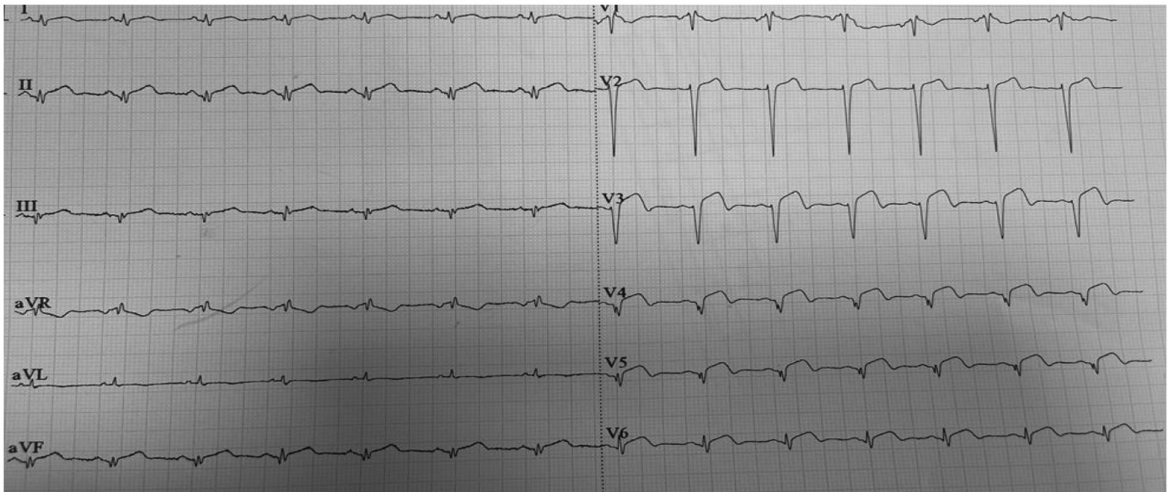

Figure 4. Electrocardiography

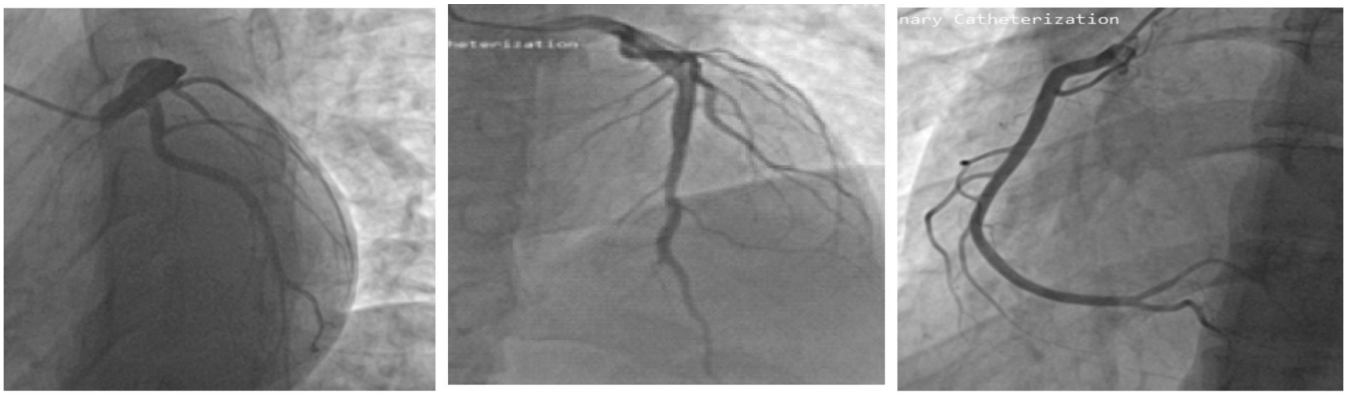

Figure 5. Coronary angiography

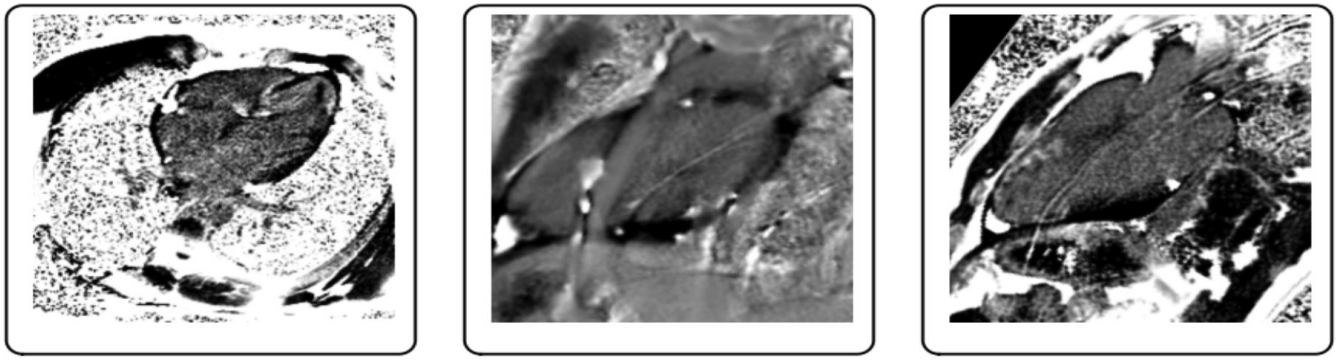

Figure 6. Cardiac MRI
MRI: Magnetic resonance imaging

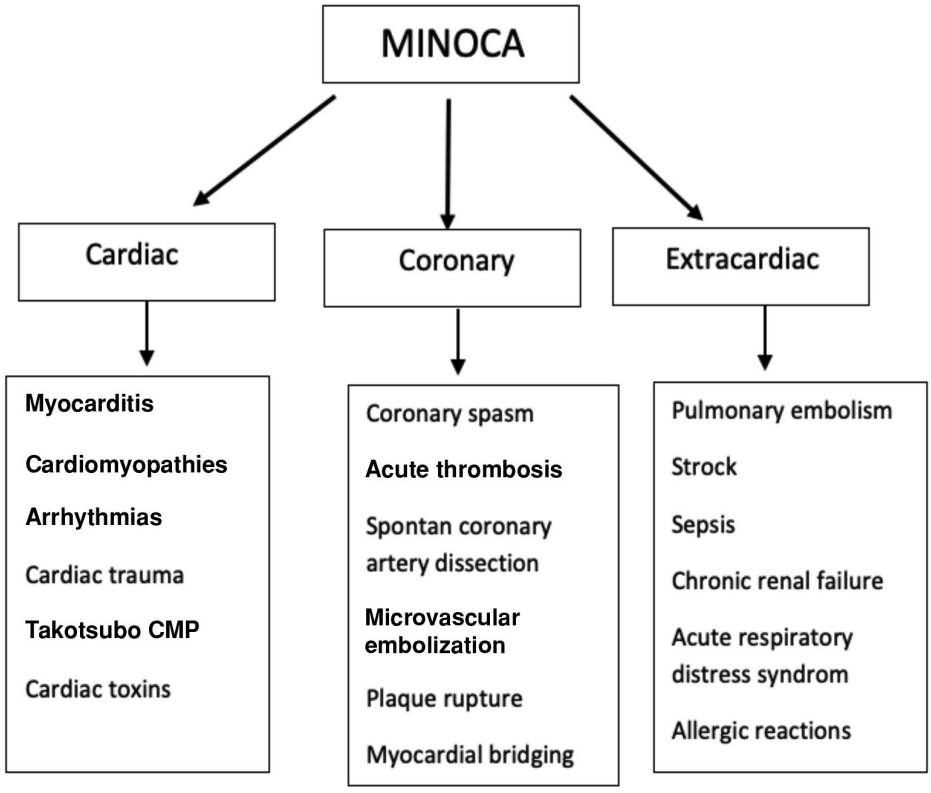

Figure 7. MINOCA

DISCUSSION

MINOCA is a syndrome with features of myocardial infarction but no significant stenosis (i.e., less than 50%) on coronary angiography [2]. Rupture of atheroma in the coronary artery due to sudden stress and other reasons, along with platelet adhesion and aggregation, causes thrombus formation. Troponin levels can also be elevated because of myocardial damage that occurs when a vessel is completely occluded. Patients with MINOCA tend to be younger and are more common in women. Evidence to date has established that coronary arterial function and disease are not limited to obstructive CAD in women [3]. Coronary angiography is essential to establish the diagnosis, and the underlying cause should be investigated. These causes are divided into coronary artery-related, cardiac, and extracardiac. 5-10% of common myocardial infarctions are MINOCA (Figure 7) [4].

The signs and symptoms are the same as those of a heart attack in someone who has blocked arteries-chest discomfort (pain, pressure, tightness), shortness of breath, nausea, and lightheadedness. There are some shared risk factors high blood pressure, high cholesterol, diabetes, and smoking-but they are less frequent in MINOCA patients than in patients who have had heart attacks with obstructive coronary disease.

MINOCA has a lower mortality rate than myocardial infarction with CAD. If the cause of MINOCA cannot be determined by coronary angiography, left ventriculography or non-invasive methods are recommended. Cardiac MR tomography is one of the main tools used to rule out the underlying cause of MINOCA. The pathophysiology of the disease has been better understood using intracoronary imaging (intravascular ultrasound and optical coherence tomography) studies [5].

Spontaneous coronary artery dissection: Spontaneous CAD is more common in women between the ages of 45 and 55 years. It can be observed in women who use oral contraceptives and have a history of infertility during or before menstruation or during infertility treatment [6]. If there is no hemodynamic disorder, conservative treatment is preferred. Treatment for pregnant women is the same as that for non-pregnant women.

Takotsubo cardiomyopathy: Takotsubo cardiomyopathy is more common in postmenopausal women. Clinically, it resembles acute coronary syndrome. The word "Takotsubo" is a container used by the Japanese to catch octopus, which has a circular bottom and narrow neck, which resembles the heart's condition in TC to a certain degree [7]. Therefore, response to fluctuations in the levels of adrenaline and noradrenaline secreted in moments of stress, microvascular disorder, and

underlying left ventricular outflow tract obstruction can be indicated.

Micro-macrovascular dysfunction: Microvascular dysfunction and coronary vasospasm are the underlying causes in 80% of patients without major stenoses on coronary angiography, and most cases are women. Studies have shown that statins, ACE inhibitors, ARBs, and beta blockers are beneficial, but dual anticoagulation therapy has been identified [8].

It is important to raise awareness of MINOCA. Educating individuals about symptoms, risk factors, and available treatments may facilitate an earlier diagnosis. Even after long-term treatment, patients with MINOCA are still at risk of future cardiovascular events. Lifestyle changes, medications, and regular follow-up are important components of treatment.

Ethics

Informed Consent: The patients written informed consent was obtained.

Authorship Contributions

Surgical and Medical Practices: G.A., N.I., A.S., Concept: G.A., N.I., A.S., Design: G.A., N.I., A.S., Data Collection or Processing: G.A., N.I., A.S., Analysis or Interpretation: G.A., N.I., A.S., Literature Search: G.A., N.I., A.S., Writing: G.A., N.I., A.S.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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CASE REPORT

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Approach to Breast Lesions with Radiology-pathology Discrepancy: Discussion Based on 3 Cases Diagnosed with Malignancy After Surgery

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ABSTRACT

Breast lesions are mainly classified as benign and malignant. When breast cancer is diagnosed, the patient is evaluated and a treatment plan is prepared. For benign lesions, follow-up or surgery may be performed. Imaging and biopsy results are essential when deciding on surgery. In particular, when there is a discrepancy between radiologic imaging and pathology results, excision may be useful for definitive diagnosis. We planned to present an approach to suspicious breast lesions with radiology pathology discordance through the presentation of three patients diagnosed with malignancy. Between February 2018 and March 2023, patients who underwent wire marking and excision for suspicious breast lesions were analyzed. Three patients diagnosed with malignancy after total excision were analyzed in detail. Of 33 patients, 2 (6.06%) patients had ductal carcinoma *in situ* and 1 (3.03%) patient had invasive tubular carcinoma. Preoperative and postoperative pathological findings were consistent with benign changes in all three cases. After total excision, a definitive diagnosis was made, and follow-up and treatment were planned. In cases of radiology-pathology discordance, total excision may be effective in detecting atypia, carcinoma *in situ*, or invasive carcinoma not detected on pathologic examination. Therefore, even if the biopsy result is not malignant, wire-guided total excision of radiologically suspicious lesions should be considered as a diagnosis and treatment method.

Keywords: Breast lesions, cancer, excision

INTRODUCTION

Breast cancer is the most common malignancy in women [1,2]. Early diagnosis and treatment are important. Therefore, annual physical examination, mammography, and ultrasonography, especially in women starting from the age of 40 years, are important for early diagnosis. Thus, the morbidity and mortality rates related to breast cancer can be reduced [3]. Thanks to routine screening, not only malignancies but also lesions with suspected malignancy can be detected and treated.

Non-malignant, epithelial benign lesions of the breast. Papillomas, adenosis, fibroadenomas, sclerosing lesions, and florid hyperplasia are examples of these lesions. Especially in proliferative lesions with atypia, there is an increased lifetime risk for breast cancer [4]. Therefore, even if the preliminary diagnosis is benign, the mass in the breast should be closely followed up. Excision should be planned when biopsy and imaging results are discordant and atypia is detected. In this way, even if the biopsy result is benign, atypia *in situ* or invasive ductal carcinomas that could not be detected in the biopsy can be diagnosed after the total excision of the mass. With the cases we present, we demonstrated that early stage malignancy can be diagnosed by excision of lesions with discordant radiologic pathology.

Between February 2018 and April 2022, 70 patients who underwent surgery for breast mass in our clinic were evaluated. Thirty-three patients who were radiologically suspicious on breast imaging but whose biopsy results were found to be benign and who were decided to be excised due to persistence of clinical suspicion of malignancy (continued suspicion in control radiology examinations, family history) were analyzed in detail. Clinical data of three patients diagnosed with malignancy were recorded.

The article has been presented previously in a scientific meeting orally (1st International 4th National Breast Surgery Congress).

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CASE PRESENTATION

When 33 patients were reviewed, it was found that 9 (27.2%) patients had intraductal papilloma (IDP), 21 (63.6%) patients had benign proliferative and non-proliferative pathologies (8 patients had fibroadenoma, 4 patients had apocrine metaplasia, 3 patients had ductal hyperplasia, 2 patients had phyllodes tumor, 2 patient had atypical papilloma, 1 patients had sclerosing papilloma, 1 patients had hamartoma), 2 (6.06%) patients had ductal carcinoma *in situ* (DCIS), and 1 (3.03%) patient had invasive tubular carcinoma (Table 1). The mean age of the 33 patients was 48 (27-70).

When the three patients diagnosed with malignancy were examined in detail, the mean age was 61.3 years, and intraoperative frozen section analysis of all patients did not reveal malignancy. Biopsy and frozen section analysis of patients whose pathological examination resulted in DCIS were compatible with IDP. One patient who was later diagnosed with tubular carcinoma had a frozen section result of sclerosing adenosis.

The ages of the patients whose pathology was DCIS were 67 and 61. Two patients were postmenopausal and had no family history of malignancy. While the largest lesion in one of the patients was 17 mm in diameter (Figure 1), the other patient had a mass of 8 mm diameter. Both patients had a history of bloody nipple discharge. Preoperative and intraoperative pathological diagnoses of two patients were IDP. DCIS was diagnosed in the postoperative evaluation of excised tissue. Patients received radiotherapy during the postoperative period. No recurrence was found at the 6-month follow-up.

The third patient was 56 years old. She had a 4 mm lesion that was diagnosed as invasive tubular carcinoma. The frozen section result of this patient showed sclerosing adenosis (Table 1). This patient also had no family history of breast cancer.

DISCUSSION

Cancer is one of the leading causes of death worldwide. Breast cancer is the most common cancer among women and is one of the leading causes of death in women [5]. As with all types of cancer, early diagnosis and treatment are important in breast cancer. Therefore, early detection and treatment of suspicious lesions are possible with the development of screening programs.

Radiological imaging is critical to breast examination as a complementary element to physical examination. Ultrasonography and/or mammography findings are especially important in non-palpable lesions in the breast. Even if the biopsy result of a suspicious lesion is benign, in which case the radiology-pathology result is non-correlated, it is important to consider total excision to exclude or diagnose a possible malignancy [6].

Benign breast diseases comprise a heterogeneous group that includes developmental anomalies, inflammatory lesions,

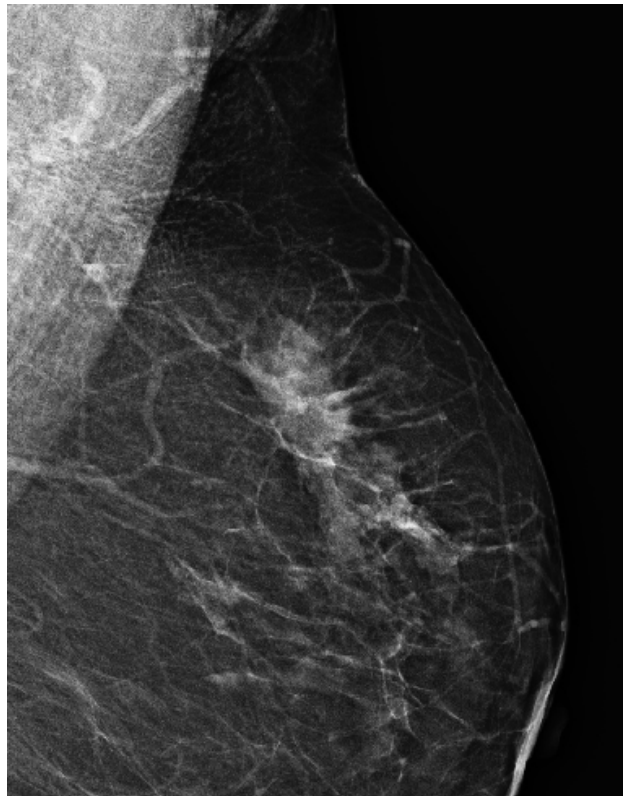

Figure 1. Lesion in the upper outer quadrant of the left breast

Table 1. Outcomes of patients diagnosed with malignancy

Patient	Gender	Age	Mammography findings	Ultrasound findings	MRI findings	Preoperative diagnosis	Postoperative diagnosis	Tumour size (diameter)	Treatment
1	Female	67	BIRADS 0*	BIRADS 4C	No pathology	DH **	DCIS***	8 mm	RT****
2	Female	61	BIRADS 4	BIRADS 4C	BIRADS 4	IDP*****	DCIS**	17 mm	RT****
3	Female	56	BIRADS 4	BIRADS 4B	BIRADS 4	Sclerosing adenosis	Invasive tubuler carcinoma	4 mm	Close follow-up

*Breast Imaging Reporting and Data Systems, **Ductal hyperplasia ,***Ductal carcinoma *in situ*, ****Radiotherapy, *****Intraductal papilloma, MRI: Magnetic resonance imaging

and epithelial and stromal proliferations. These diseases may present with various symptoms or may be detected incidentally by imaging and microscopy. Examples of these lesions include hyperplasic lesions, cysts, fibroadenomas, IDPs, sclerosing adenosis, radial scars, fat necrosis, mastitis, and ductal ectasia [7].

Epithelial lesions can be examined in three main categories: non-proliferative, proliferative without atypia, and proliferative with atypia. While the lifetime risk of developing invasive carcinoma is 5-7% in non-proliferative and proliferative lesions without atypia, it increases up to 13-17% in lesions with atypia [4].

Papillary breast lesions comprise a group of clinically, histologically, and biologically heterogeneous breast diseases [8]. Papillary lesions of the breast are a diagnostic entity that includes benign papillomas, papillomas with focal epithelial atypia, DCIS, lobular neoplasia, encapsulated papillary carcinomas with or without invasion, solid papillary carcinomas, and invasive papillary carcinomas. IDPs are benign intraluminal proliferations lined with a population of basal and luminal cells [9]. Most papillomas appear in the perimenopausal period between the ages of 30 and 50. They may not always be seen on mammography, and when seen, they may be observed as calcification [10]. After diagnosing papilloma on biopsy, the risk of concomitant DCIS is primarily determined by the detection (or absence) of atypical epithelial proliferation. After biopsy, the risk of upgrade after excision of papilloma without atypia is 2-3% [11]. Considering that some studies have shown that it may increase up to 5-10% after excision of IDP, it would be appropriate to plan the excision by evaluating it together with imaging features [12].

Clinical symptoms in the parameters found to be significantly associated with upgrade include nipple discharge and/or a palpable mass, large size of the lesion (>1-1.5 cm), contralateral breast carcinoma, multifocality, and peripheral localization. In some studies, advanced age was also found to be a factor [13-15]. In this case presentation, malignancy was found in 3 of 33 patients (9.09%) in whom excision was recommended in accordance with the literature.

In conclusion, proliferative lesions of the breast are benign lesions. However, considering that the possible atypia in these lesions cannot be detected by any imaging method and the possibility of atypia or carcinoma *in situ* in the final pathology result, we believe that excision is important in terms of diagnosis and treatment, especially in cases of radiology-pathology discordance.

Ethics

Informed Consent: Constent was obtained from the patients.

Authorship Contributions

Surgical and Medical Practices: S.E.B., L.D.E., Concept: S.E.B., L.D.E., Design: G.E., L.D.E., Data Collection or Processing: S.E.B., G.E., Analysis or Interpretation: S.E.B., G.E., L.D.E., Literature Search: S.E.B., Writing: S.E.B., G.E., L.D.E.

Conflict of Interest: No conflict of interest was declared by the authors.

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CASE REPORT

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Temporomandibular Joint Internal Derangement: A Case Report and Literature Review

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ABSTRACT

This case report presents a patient with temporomandibular joint dysfunction, focusing on radiological, and clinical findings that contributed to the diagnosis and treatment plan. The use of imaging modalities played a significant role in understanding the underlying pathology and guiding the management of patients.

Keywords: Temporomandibular joint, TMJ internal derangement, magnetic resonance imaging, TMJ internal derangement management

INTRODUCTION

The temporomandibular joint (TMJ) is a ginglymoarthrodial synovial joint that allows both backward and forward translation and gliding motion. The articular surfaces of the TMJ are formed inferiorly by the mandibular condyle and superiorly by the glenoid fossa (also known as mandibular fossa) and the articular eminence of the temporal bone. What makes this joint unique is that its articular surfaces are covered by fibrocartilage instead of hyaline cartilage [1].

The TMJ disk is a biconcave fibrocartilaginous structure that interposes between the mandibular condyle and the articular surface of the temporal bone. This interposition of the disc between the two bony portions of the joint has the important function of preventing joint damage. In addition, the disc facilitates the sliding of the mandibular condyle in relation to the temporal bone during the opening and closing of the mouth [2].

The main cause of temporomandibular joint dysfunction (TMD) is internal derangement of the joint, defined as an abnormal relationship between the articular disk and the mandibular condyle that interferes with the normal biomechanics of the TMJ and can manifest clinically as joint pain, jaw deviation while opening the mouth, or sounds (e.g., clicks) emanating from the joint [3].

CASE PRESENTATION

This case report describes a 42-year-old female patient with TMJ dysfunction, focusing on radiological and dental findings that contributed to the diagnosis and treatment plan. The patient exhibited a range of symptoms, including ear pain, joint discomfort, cervical pain, and bruxism, all of which were found to be associated with TMJ dysfunction. The use of imaging modalities, along with comprehensive dental evaluation, is crucial in understanding the underlying pathology and guiding the management of the patient.

The patient underwent a series of examinations by multiple specialists. ENT analysis revealed vasomotor rhinitis, which could contribute to nasal congestion, further complicating TMJ dysfunction. Increased acid levels, detected through gastroenterological analysis, likely added to the patient's stress levels and could intensify TMJ symptoms. It should also be noted that long-term regurgitation can lead to tooth erosion, reduced tooth height, and subsequently, increased stress on the TMJ. Endocrinological evaluation revealed the presence of Hashimoto syndrome, which may have contributed to overall systemic imbalances affecting the TMJ. Dental assessment revealed that the principles of overbite and overjet had been violated, resulting in limited space for the anterior teeth of the lower jaw. This caused the anterior teeth to break, as the patient complained.

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When we asked the patient to open a mouth, the lower jaw deviated to the left side at 27 mm (Figure 1). The maximum opening deviation disappeared and a painful situation was present on both sides, accompanied by bilateral TMJ clicking.

During intraoral screening, the patient was diagnosed with class 1 malocclusion. During examination, the patient denies any history of direct or indirect trauma in the orofacial area. A postural probe revealed shoulder dystonia, flat foot, and asymmetry in hand position, suggesting potential muscular imbalances and compensatory mechanisms. Palpation revealed tender masseter muscles, trapezius muscles, and the anterior portion of the temporal muscle, indicating possible myofascial pain related to TMJ dysfunction.

Follow our recommendation, the patient underwent TMJ magnetic resonance imaging (MRI) examination to clarify the diagnosis (Figure 2).

Figure 1. When we asked the patient to open her mouth, the lower jaw deviated to the left side at 27 mm. The maximum opening deviation disappeared and a painful situation was present on both sides, accompanied by bilateral TMJ clicking

TMJ MRI revealed findings consistent with bilateral TMJ anterior disk displacement with reduction, no joint effusion, and no visible osteoarthritic changes.

After conducting an MRI examination and a thorough medical history review, the final diagnosis of TMD was established, and treatment was initiated. The therapeutic approach was thoroughly explained to the patient, and a special informed consent form was signed.

Dental treatment involved manual muscle deprogramming, during which supracontacts were identified and reduced, and overactive and spasmodic muscles were relaxed and retained. Because of mouth breathing, the palate was partially adapted, and the jaw was deprogrammed and repositioned. Dietary advice included avoiding hard foods to reduce muscle strain. Cervicogenic headache was managed with analgesics (ibuprofen, 10 mg/kg/day orally, every 8 hours), and she was recommended to maintain a good posture while sitting and standing and refrain from sleeping on her stomach to reduce the strain on the neck muscles and ligaments. The patient was advised to switch the pillow to a softer one and to place a rolled towel under the neck while sleeping. It was recommended to normalize the sleeping routine to regulate the nervous system function and thereby increase the patient's stress resilience (Figure 3).

In addition, an intraoral impression was taken, and an intraoral removable hard occlusal splint was fabricated in the laboratory to help reposition the jaw and alleviate muscle tension. The patient was instructed to wear the splint for a minimum of 12 h daily, particularly during the night.

The patient attended three follow-up appointments over a 1 month period. Deviation was corrected, pain was reduced, and ear noise diminished (Figure 4).

A follow-up MRI examination was recommended 3 months later to assess the progress and effectiveness of the treatment. The use of the repositioning splint resulted in proper jaw alignment, with no evidence of deviation.

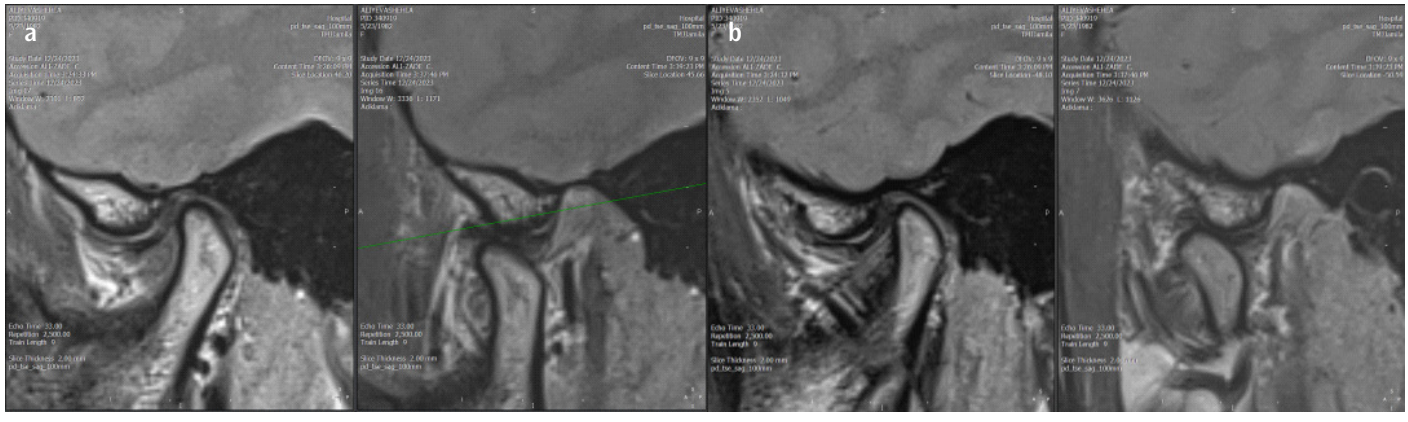

Figure 2. (a) Right TMJ, (b) left TMJ

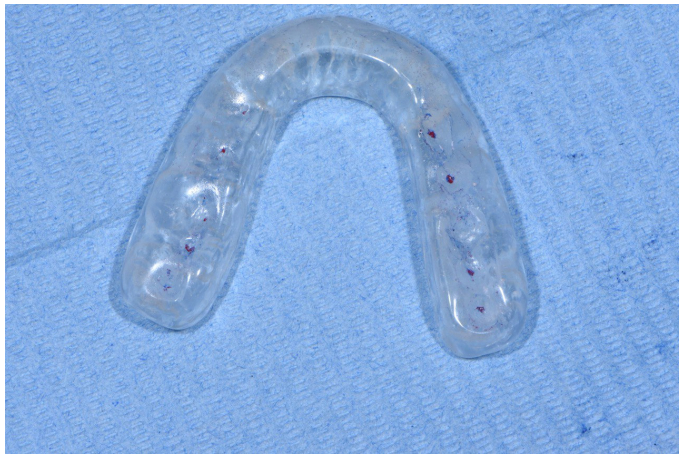

Figure 3. Occlusal hard splint used as treatment for TMD

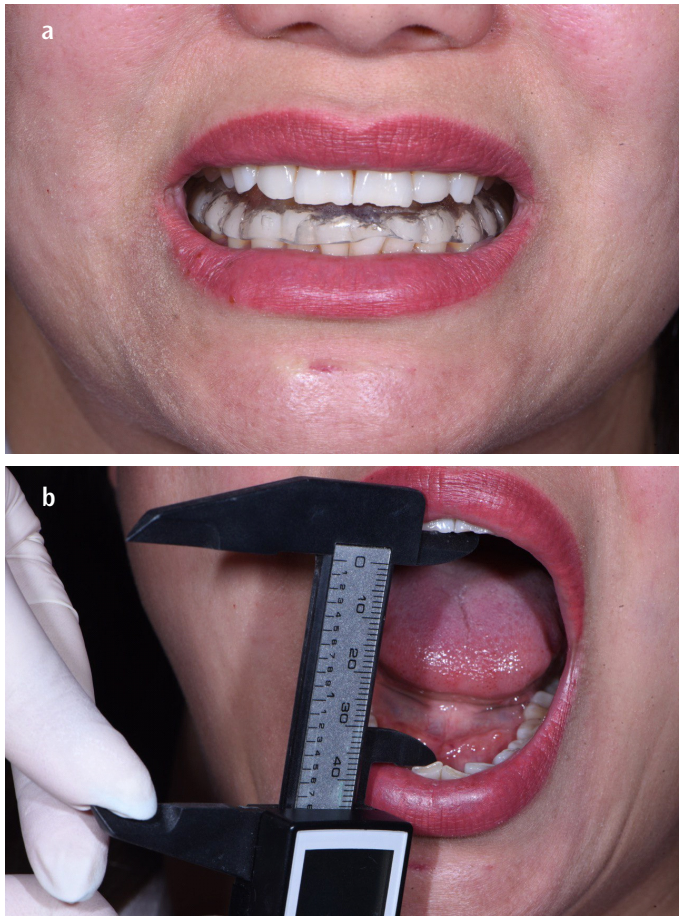

Figure 4. (a) Front view of occlusal splint, (b) posttreatment, taken after 3 months of follow-up

DISCUSSION

The TMJ is considered a complex synovial articulation and the most used joint in the human body [4].

TMD encompasses a range of clinical problems such as chronic jaw pain, restricted mandibular movement, clicking or popping sounds during jaw movement, headaches, ear pain or tinnitus, dental issues such as worn or broken teeth, and disruptions in sleep, affecting overall quality of life and well-being.

An exhaustive clinical assessment is imperative, including mandibular range of motion evaluation, TMJ palpation (including ligaments and capsule structures), masticatory musculature (temporalis and masseter) pain under pressure, load testing, and sound detection (clicking, crepitus, and hard-tissue grating) [5].

In conclusion, while clinical examination forms the cornerstone of TMD diagnosis, the role of imaging, particularly MRI, has become increasingly significant in both the diagnosis and management of TMD. This case highlights the importance of timely MRI diagnosis in TMD. It not only confirmed the clinical suspicion but also provided detailed anatomical and pathological information essential for appropriate treatment planning. The correlation between the patient's symptoms and radiological findings further emphasizes the value of MRI as a tool to bridge the clinical-radiological gap in TMD assessment. Moreover, the ability of MRI to detect subtle articular and soft tissue changes in the TMJ underscores its high sensitivity in diagnosing TMD-related pathology.

Ethics

Informed Consent: Informed consent form was signed.

Authorship Contributions

Surgical and Medical Practices: J.A.Z., A.K., Concept: J.A.Z., A.K., Design: J.A.Z., A.K., Data Collection or Processing: J.A.Z., A.K., Analysis or Interpretation: J.A.Z., A.K., Literature Search: J.A.Z., A.K., Writing: J.A.Z., A.K.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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CASE REPORT

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We Say "Reunite with Your Pure Heart" to our Patient who Will Undergo Kidney Transplantation

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ABSTRACT

Permanent hemodialysis catheters are reguarly used in stage V chronic kidney disease patients undergoing hemadialysis, but their long stay in the body can result in infection, sepsis and thrombus formation in the right atrium. Hemodialysis catheter-related right atrial thrombus is a rare complication but can lead to serious complications. Intracardiac thrombus can be asymptomatic in hemodialysis patients, and it can manifest itself with fever, shortness of breath, chest pain, and even sudden death due to pulmonary embolism.

Keywords: Catheter-related right atrial thrombus, hybrid operation, kidney transplantation, hemodialysis

INTRODUCTION

Permanent hemodialysis catheters are commonly used in stage V chronic kidney disease (CKD) patients undergoing hemadialysis, but their long stay in the body can result in infection, sepsis, and thrombus formation in the right atrium [1]. Hemodialysis catheter-related right atrial thrombus is a rare complication that can lead to serious complications. Intracardiac thrombus can be asymptomatic in hemodialysis patients and manifest as fever, shortness of breath, chest pain, and even sudden death due to pulmonary embolism [2,3].

CASE PRESENTATION

A 34-year-old male patient with long-standing complaints of nausea, shortness of breath, and high blood pressure developed end-stage CKD due to glomerulonephritis. For 4 months, the patient has been undergoing hemodialysis through the right internal jugular catheter with the diagnosis of CKD stage V. On 16.11.2022, the patient applied to the hospital for a kidney transplant operation, and preparations for the operation were started. On that date, the patient was asked to consult a cardiologist before transplantation. Vitals were normal, cre-8.5, sinus tachycardia on electrocardiogram, left ventricle ejection fraction-55% on echo, and a hyperechogen mass of 38, 16 mm was observed inside the right atrium (thrombus?- TEE is recommended). It was decided to treat with Clexane 0.4 mL 2 subcutaneous preparation for 2 weeks. Because no reduction in the size of the mass was observed after the treatment, TEE was performed on 01.12.2022.

A hyperechogen, uneven 38 20 mm mass (thrombus? Derivation?) attached to the lateral wall with a wide leg between the inferior vena cava and superior vena cava was observed in the right atrium. Cardiac computed tomography (CT) is performed on the patient for differentiation, and a wide-based, irregular, hypodense, non-contrast, homogeneous intracardiac mass of 35.0, 20.0, 34.0 mm, bulging from the posteroinferior wall of the right atrium to the RA orifice is observed (the CT image is more in favor of a right atrial thrombus). The patient is advised to consult a cardiologist, and based on the opinion of the council, it is decided to perform both operations at the same time. On 15.12.2022, a hybrid operation-first "thrombus removal from the right atrium", then "right sided laparoscopic donor nephrectomy" was performed and the removed kidney was successfully transplanted into the right retroperitoneal area. Because of pathohistological examination of the mass, it was confirmed to be a thrombus. After 1 week, the patient was sent home under outpatient observation (cre 1.36). The patient is continuously monitored by us. In the echo examination, no pathological changes were detected in the patient's clinical complaints.

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DISCUSSION

According to recent studies, right atrial thrombosis associated with permanent hemodialysis catheter is found in 8% of patients with CKD. The specificity of echo examination in the detection of thrombus is 86% and its sensitivity is 95% [4]. Right atrial thrombus is divided into two types. Type I is of deep venous thrombosis origin and is prone to thromboembolism. Type II thrombus is formed in the atrium with a foreign body such as a central venous catheter, is usually inactive, and has a lower risk of mortality [5].

In the patient we present, despite 2 weeks of anticoagulant therapy, the size did not shrink, leading to a rejection of the diagnosis of thrombus, and cardiac CT focused on a calcified thrombus mass. The absence of a malignant mass of the mentioned derivative did not prevent its removal by joint surgery. Histopathology confirmed that the mass was a thrombus.

Educational issues

1. Patients with indwelling hemodialysis catheters should undergo regular echo examination to prevent complications that may occur in the future (e.g ischemic stroke due to thromboembolism, pulmonary embolism).

2. Implementation of hybrid heart operations with transplantation in China possible.

Ethics

Informed Consent: Patient consent was obtained.

Authorship Contributions

Surgical and Medical Practices: S.S., R.S., Concept: S.S., R.S., Design: S.S., R.S., Data Collection or Processing: S.S., R.S., Analysis or Interpretation: S.S., R.S., Literature Search: S.S., R.S., Writing: S.S., R.S.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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