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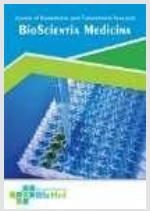

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Recurrent Dermatofibrosarcoma Protuberans with Fibrosarcomatous Transformation: A Case Report

Haivan Kusuma Aji[1*], Kiki Akhmad Rizki[2]

[1]Surgical Oncology Trainee, Head, Neck and Surgical Oncology Division, General Surgery Department, Universitas Padjadjaran/Dr. Hasan Sadikin General Hospital, Bandung, Indonesia

[2]Surgical Oncology Consultant, Head, Neck and Surgical Oncology Division, General Surgery Department, Universitas Padjadjaran/Dr. Hasan Sadikin General Hospital, Bandung, Indonesia

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***Corresponding author:**
Haivan Kusuma Aji

E-mail address:
haivankusumaadji@gmail.com

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A B S T R A C T

Background: Dermatofibrosarcoma protuberans (DFSP) is a rare cutaneous sarcoma with a propensity for local recurrence but a low risk of distant metastasis. Fibrosarcomatous transformation (FS-DFSP) is a rare but aggressive variant associated with increased metastatic potential. **Case presentation:** We present the case of a 39-year-old male with recurrent DFSP involving the scalp, mandible, and humerus, complicated by fibrosarcomatous transformation and distant metastases to the lungs and bones. The patient underwent multiple excisions, radiation therapy, and systemic treatments including chemotherapy and imatinib, but ultimately experienced disease progression. **Conclusion:** This case highlights the challenges in managing recurrent DFSP with fibrosarcomatous transformation. The rarity of this entity necessitates a high index of suspicion for early diagnosis and aggressive multidisciplinary management to improve patient outcomes. Further research is needed to identify effective treatment strategies for this aggressive variant of DFSP.

1. Introduction

Dermatofibrosarcoma protuberans (DFSP) stands as an uncommon, slow-growing cutaneous sarcoma that originates in the dermis and infiltrates into the subcutaneous tissue. The tumor is characterized by its locally aggressive behavior, demonstrating a high propensity for local recurrence but a relatively low risk of distant metastasis. The estimated incidence of DFSP ranges from 0.8 to 4.5 cases per million individuals annually, constituting less than 1% of all soft tissue sarcomas. The clinical presentation of DFSP typically involves a painless, indurated plaque or nodule situated on the trunk or extremities, often with a history of gradual enlargement over several years. The insidious nature of its growth often leads to delayed diagnosis and treatment, contributing to the challenges in its management. The standard therapeutic approach for localized DFSP centers on wide local excision with the attainment of clear margins. This surgical strategy has been shown to significantly diminish the risk of local recurrence. However, even with meticulous surgical resection, local recurrence rates can still vary between 10% and 50%, underscoring the difficulties in achieving complete tumor eradication. The intricate growth pattern of DFSP, with its microscopic extensions

beyond the clinically apparent margins, poses a significant challenge to surgeons aiming for complete resection. The incomplete removal of these microscopic extensions can serve as a nidus for future recurrence, necessitating vigilant follow-up and potential re-excision.[1,2]

In a subset of DFSP cases, a phenomenon known as fibrosarcomatous transformation (FS-DFSP) can occur. This transformation is marked by the emergence of a high-grade sarcomatous component within the tumor, typically fibrosarcoma. FS-DFSP is associated with a more aggressive clinical course, characterized by an elevated risk of distant metastasis and a less favorable prognosis compared to conventional DFSP. The underlying mechanisms driving fibrosarcomatous transformation remain an area of active investigation, but it is believed to involve a complex interplay of genetic and epigenetic alterations that disrupt the normal growth and differentiation of tumor cells. The acquisition of these alterations confers upon the tumor cells a heightened capacity for invasion, metastasis, and resistance to therapy, contributing to the challenges in its management. The diagnosis of FS-DFSP hinges upon histopathological examination, which reveals the presence of a high-grade sarcomatous component within the tumor, typically fibrosarcoma. The distinction between FS-DFSP and other spindle cell sarcomas can be aided by immunohistochemical staining, which can highlight specific markers associated with fibrosarcoma. The identification of fibrosarcomatous transformation carries significant prognostic implications, as it is linked to a considerably worse prognosis, with 5-year survival rates ranging from 30% to 50%. This underscores the critical importance of accurate and timely diagnosis to guide appropriate therapeutic decision-making. The management of FS-DFSP presents a formidable challenge and often necessitates a multidisciplinary approach involving collaboration among surgeons, oncologists, radiation therapists, and pathologists. Wide local excision with the achievement of clear margins remains the cornerstone of treatment for localized tumors. However, given the elevated risk of local recurrence and distant metastasis, the integration of adjuvant therapies such as radiation therapy and systemic therapy may be warranted. The selection of adjuvant therapies is guided by various factors, including the extent of the disease, the presence of metastatic spread, and the patient's overall health status. Radiation therapy has demonstrated efficacy in reducing the risk of local recurrence in DFSP, particularly in scenarios where surgical margins are close or positive. The precise radiation dose and fractionation schedule for FS-DFSP remain to be definitively established, but doses ranging from 50 to 60 Gy are commonly employed. Radiation therapy exerts its therapeutic effect by damaging the DNA of tumor cells, thereby impeding their ability to proliferate and survive. However, radiation therapy is not without its potential side effects, which can include skin reactions, fatigue, and damage to surrounding healthy tissues. The careful planning and delivery of radiation therapy are essential to maximize its benefits while minimizing its potential harms.[3-5]

Systemic therapy options for FS-DFSP are currently limited. Conventional chemotherapy has exhibited limited efficacy, with response rates falling below 20%. The relative chemoresistance of FS-DFSP underscores the need for novel therapeutic approaches. Targeted therapies, such as imatinib, have emerged as promising avenues for patients with advanced or metastatic DFSP. Imatinib functions as a tyrosine kinase inhibitor that targets the platelet-derived growth factor receptor beta (PDGFRB), which is frequently overexpressed in DFSP. Clinical trials have provided evidence that imatinib can elicit tumor responses in a subset of patients with advanced DFSP, encompassing those with FS-DFSP. However, the duration of response is often transient, and the development of resistance to imatinib can occur over time. The identification of biomarkers that can predict response to imatinib and the development of strategies to overcome resistance represent active areas of research.[6,7]

The intricate interplay between the tumor and the host immune system has garnered increasing attention in recent years. Immunotherapy, which harnesses the power of the immune system to recognize and eliminate cancer cells, has shown remarkable success in the treatment of various malignancies. The potential role of immunotherapy in the management of DFSP, including FS-DFSP, is an area of ongoing exploration. Preliminary studies have suggested that immune checkpoint inhibitors, which unleash the brakes on the immune system, may hold promise in the treatment of DFSP. However, further research is needed to define the optimal patient selection criteria and treatment regimens for immunotherapy in this setting.[8-10] The case presented in this report underscores the complexities inherent in the management of recurrent DFSP with fibrosarcomatous transformation. The patient's clinical course, marked by multiple recurrences, distant metastases, and ultimately the need for palliative care, highlights the aggressive nature of this disease and the limitations of current therapeutic options. The rarity of FS-DFSP poses a significant challenge to clinicians, necessitating a high index of suspicion for early diagnosis and prompt initiation of appropriate therapy. The multidisciplinary management of FS-DFSP, encompassing surgical resection, radiation therapy, systemic therapy, and potentially immunotherapy, offers the best hope for improving patient outcomes. Continued research into the molecular underpinnings of FS-DFSP and the development of novel targeted therapies are essential to advance the field and provide more effective treatment options for patients with this challenging disease.

2. Case Presentation

The patient, a 39-year-old male, initially presented in 2016 with a progressively enlarging mass in the right occipital region of his scalp. The mass exhibited a gradual increase in size, with an estimated doubling time of 44 days, indicating a relatively slow but persistent growth pattern. In addition to the scalp mass, the patient also reported an ulcer in the left buccal region that had subsequently led to swelling of the left mandible. This mandibular swelling also demonstrated a progressive growth pattern, with a doubling time of 33 days, suggesting a more rapid expansion compared to the scalp lesion. The patient's medical history was further complicated by a sudden fracture of the right humerus that occurred while lifting a gallon of water, raising suspicion of potential bone involvement. Driven by these concerning symptoms, the patient sought medical attention at two different hospitals in Bandung, Indonesia. At these hospitals, biopsies were performed on the masses located in the right occipital region, left mandible, and right humerus. The biopsy specimens underwent histopathological examination, which revealed a diagnosis of dermatofibrosarcoma protuberans (DFSP). The presence of DFSP in multiple anatomical locations, including the scalp, mandible, and humerus, suggested a multifocal or potentially metastatic disease process.

Following the diagnosis of DFSP, the patient underwent two tumor excision surgeries in 2019 and 2020. The surgical procedures aimed to remove the macroscopic tumor burden and achieve clear margins to minimize the risk of local recurrence. Postoperative radiation therapy was planned as an adjuvant treatment modality to further reduce the risk of recurrence. However, the implementation of radiation therapy was unfortunately delayed due to the challenges posed by the COVID-19 pandemic, which disrupted healthcare services globally. In 2021, the patient was referred to Hasan Sadikin General Hospital for further evaluation and management. Upon physical examination, a palpable mass measuring 5x5 cm was identified in the right occipital region. The mass exhibited characteristic features of DFSP, including a firm and dense consistency, poorly defined borders, and the absence of ulceration. An intraoral examination revealed a substantial mass in the left mandibular region, measuring 6x5x5 cm. This mass also displayed a firm and dense consistency with unclear borders and no associated tenderness.

Furthermore, a deformity was observed in the distal third of the right humerus, corroborating the patient's history of a pathological fracture.

A comprehensive review of the patient's previous investigations, including histopathological analysis, confirmed the diagnosis of fibrosarcomatous dermatofibrosarcoma protuberans. This subtype of DFSP is characterized by the presence of a high-grade sarcomatous component, typically fibrosarcoma, within the tumor. Fibrosarcomatous transformation is associated with more aggressive clinical behavior and an increased risk of distant metastasis, portending a less favorable prognosis compared to conventional DFSP. To assess the extent of the disease and identify potential metastatic spread, the patient underwent a series of imaging studies. Thoracic imaging revealed the presence of metastases in the intrapulmonary region and the left 4th-5th ribs, indicating that the tumor had disseminated beyond its primary sites. A computed tomography (CT) scan of the head further identified soft tissue masses in the right occipital region and the left mandibular angle, both suspected to be metastatic sarcoma lesions. Additionally, an X-ray of the pelvis and lumbosacral region raised concerns for bone metastasis, suggesting widespread dissemination of the disease.

Based on the clinical, histopathological, and radiological findings, the final diagnosis was established as recurrent dermatofibrosarcoma protuberans with fibrosarcomatous transformation involving the right occipital region and left mandible, accompanied by bone infiltration and distant metastasis to the lungs and bones. The tumor was classified as stage G1T4aN1M1, reflecting its high-grade nature, extensive local involvement, regional lymph node metastasis, and distant metastatic spread. In 2021, the patient was initiated on chemotherapy, receiving a total of six cycles. This systemic treatment approach aimed to control the growth and spread of the tumor. The chemotherapy regimen resulted in a partial response, signifying a reduction in tumor burden but not complete eradication. In 2022, the treatment strategy was shifted to imatinib, a targeted therapy that inhibits the platelet-derived growth factor receptor beta (PDGFRB), which is often overexpressed in DFSP. The patient received six cycles of imatinib, which led to a further decrease in tumor size, demonstrating the efficacy of this targeted agent in this particular case.

In January 2023, external radiation therapy was administered to the left mandibular mass. This localized treatment approach aimed to target the residual tumor in the mandible and achieve further tumor regression. The radiation therapy resulted in a partial reduction of the mandibular mass, contributing to the overall management of the disease. Following radiation therapy, imatinib therapy was resumed to maintain tumor control and prevent further progression. Despite the initial positive response to imatinib, the patient eventually experienced disease progression, highlighting the challenges in managing advanced and metastatic DFSP. In an attempt to alleviate symptoms and improve quality of life, radiation therapy was administered to the metastases in the sacrum and vertebral bones. Palliative care measures were also instituted, focusing on pain management, oral hygiene maintenance, and ensuring adequate nutrition. The patient and his family received education on home care practices to prevent complications such as decubitus ulcers and contractures. Psychosocial support was provided to address the emotional and psychological impact of the disease, and a multidisciplinary team was involved in coordinating the patient's care and addressing his diverse needs. The patient's family was also counseled regarding potential end-of-life scenarios, acknowledging the gravity of the situation and facilitating open communication and informed decision-making.

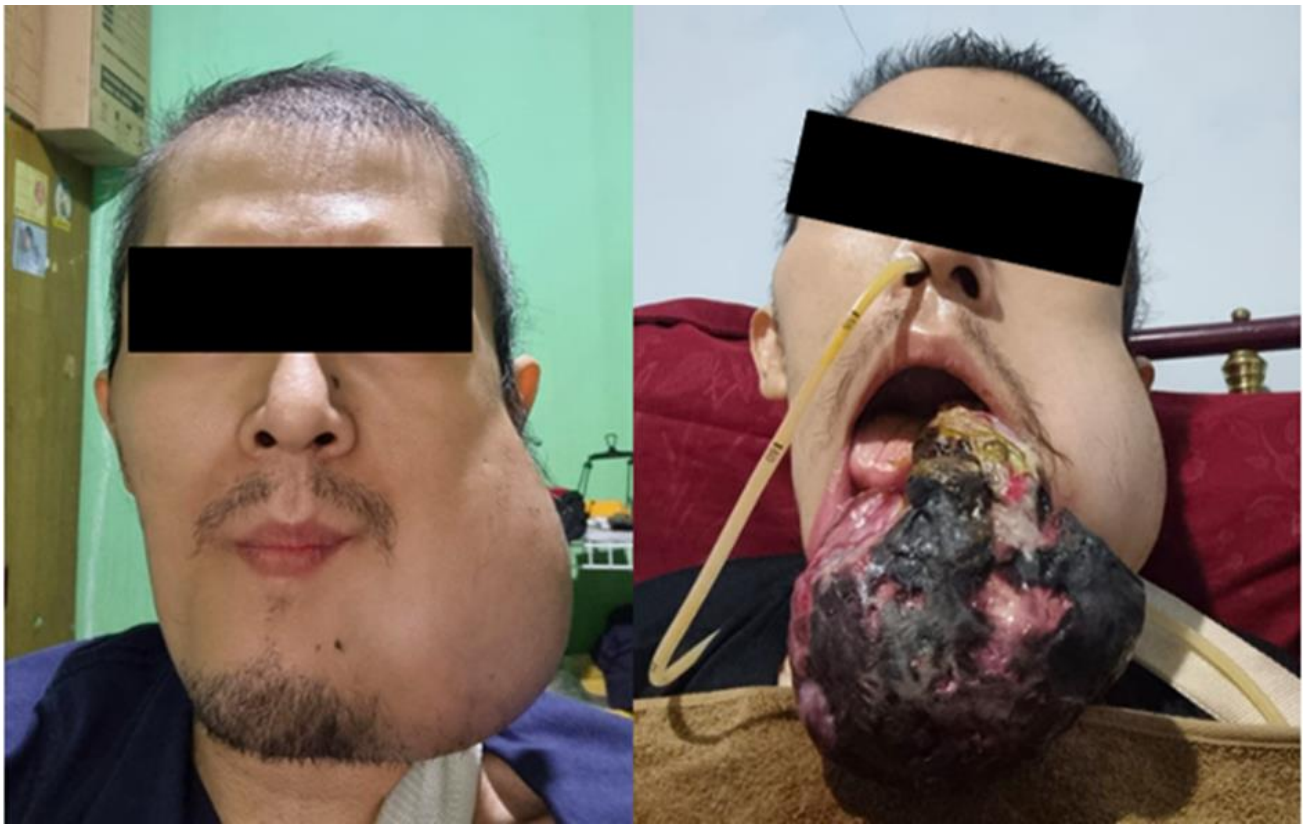

Figure 1. Large intraoral mass at left mandibular region.

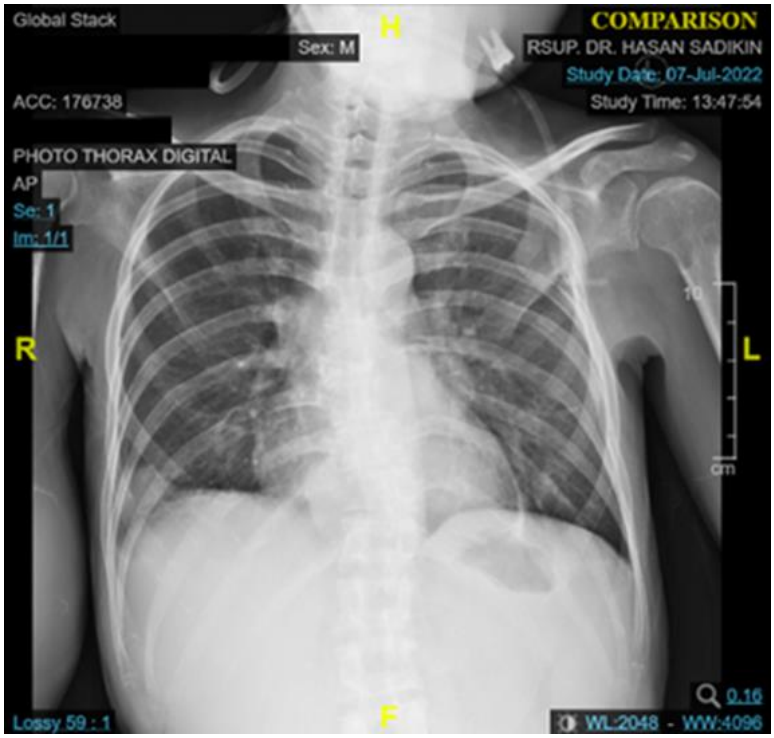

Figure 2. Intrapulmonary metastases with a suspect of metastasis bone disease.

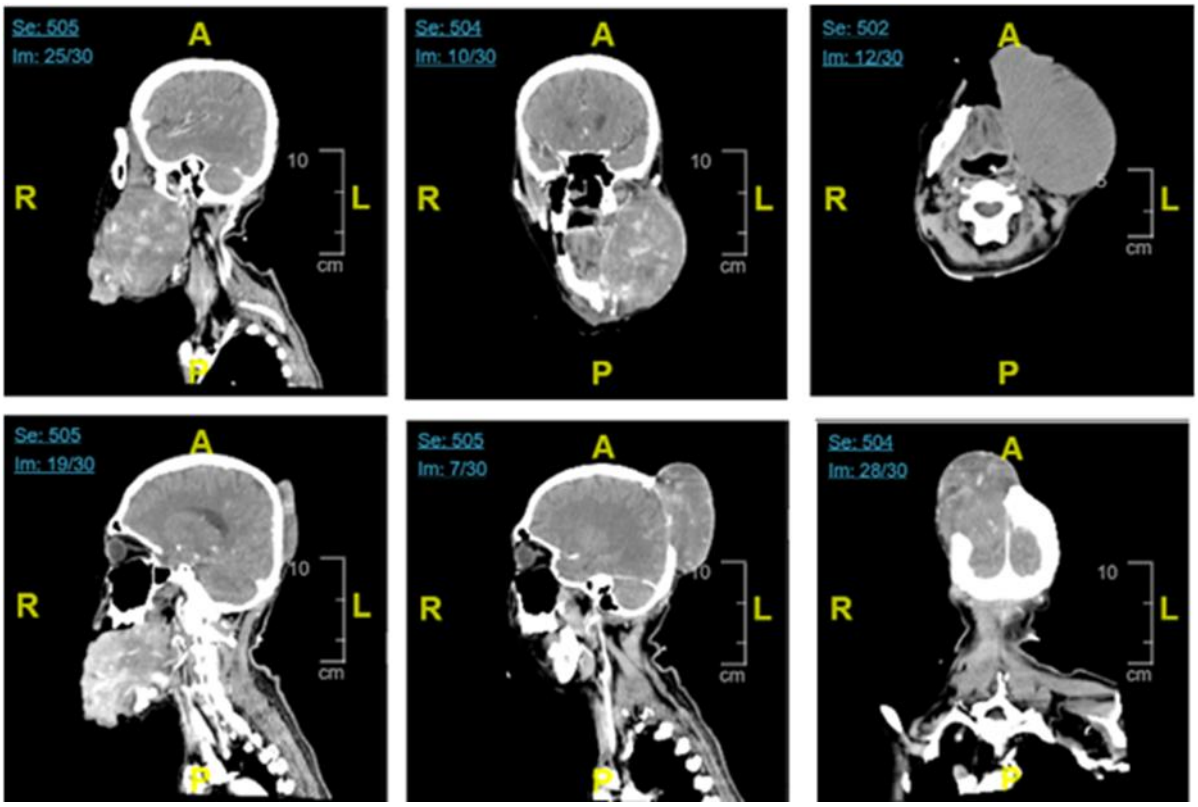

Figure 3. Destructive mass at left angle of mandible, right occipital, and right parietal.

3. Discussion

The transformation of dermatofibrosarcoma protuberans (DFSP) into its fibrosarcomatous variant (FS-DFSP) represents a perplexing and critical turning point in the disease's progression. The mechanisms underlying this transformation remain an area of intense research, with scientists striving to unravel the intricate molecular and cellular events that drive this shift towards a more aggressive phenotype. The current understanding suggests that fibrosarcomatous transformation is not a sudden event but rather a multistep process involving a complex interplay of genetic and epigenetic alterations. These alterations disrupt the delicate balance of regulatory mechanisms that govern cell growth, differentiation, and programmed cell death (apoptosis), ultimately leading to the emergence of a high-grade sarcomatous component within the tumor. The acquisition of these genetic and epigenetic changes endows the tumor cells with enhanced capabilities for invasion, metastasis, and resistance to therapy, contributing to the aggressive clinical behavior observed in FS-DFSP. The genomic landscape of FS-DFSP has been the subject of several investigations, employing techniques such as comparative genomic hybridization (CGH) and gene expression profiling. CGH studies have revealed recurrent chromosomal aberrations in FS-DFSP, including gains of chromosomes 17 and 22, as well as losses of chromosomes 9 and 13. These chromosomal abnormalities are thought to contribute to the dysregulation of critical genes involved in cell cycle control, DNA repair, and signal transduction pathways. Gene expression profiling studies have further identified alterations in the expression of various genes associated with fibrosarcomatous transformation. These genes often encode proteins involved in cell proliferation, migration, and invasion, further supporting the notion that fibrosarcomatous transformation is driven by a complex network of molecular alterations. The genetic and epigenetic alterations implicated in fibrosarcomatous

transformation are diverse and multifaceted. One of the most well-characterized genetic alterations in DFSP is the chromosomal translocation t(17;22)(q22;q13), which results in the fusion of the collagen type I alpha 1 (COL1A1) gene on chromosome 17 with the platelet-derived growth factor beta (PDGFB) gene on chromosome 22. This fusion gene leads to the constitutive activation of PDGFRB, a tyrosine kinase receptor that plays a crucial role in cell growth and proliferation. The overexpression of PDGFRB in DFSP drives tumor cell proliferation and contributes to its locally aggressive behavior. In addition to the COL1A1-PDGFB fusion gene, other genetic alterations have been identified in FS-DFSP, including mutations in tumor suppressor genes such as p53 and CDKN2A, as well as amplifications of oncogenes such as MDM2 and CDK4. These genetic alterations further disrupt the normal regulatory mechanisms governing cell growth and survival, promoting the transformation of DFSP into a more aggressive phenotype. Epigenetic alterations, which involve changes in gene expression without changes in the underlying DNA sequence, also play a crucial role in fibrosarcomatous transformation. These alterations can include DNA methylation, histone modifications, and microRNA dysregulation. Epigenetic changes can silence tumor suppressor genes or activate oncogenes, contributing to the development and progression of FS-DFSP. The identification of the molecular drivers of fibrosarcomatous transformation has significant clinical implications. The recognition of specific genetic and epigenetic alterations associated with FS-DFSP may enable the development of diagnostic and prognostic biomarkers. These biomarkers could aid in the early detection of fibrosarcomatous transformation, allowing for more timely and aggressive therapeutic intervention. Furthermore, the identification of molecular targets involved in the pathogenesis of FS-DFSP may pave the way for the development of novel targeted therapies that can specifically disrupt the signaling pathways driving tumor growth and metastasis. Despite the advances in our understanding of the molecular landscape of FS-DFSP, many questions remain unanswered. The precise sequence of genetic and epigenetic events leading to fibrosarcomatous transformation is still being elucidated. The factors that predispose certain DFSP tumors to undergo this transformation are also poorly understood. Further research is needed to identify additional genetic and epigenetic alterations involved in this process and to elucidate the complex interactions between these alterations. The development of experimental models that recapitulate the process of fibrosarcomatous transformation would provide invaluable tools for studying the underlying mechanisms and testing novel therapeutic approaches. These models could also be used to identify potential biomarkers that can predict the risk of transformation and guide the selection of appropriate treatment strategies. The enigma of fibrosarcomatous transformation in DFSP continues to challenge researchers and clinicians alike. The ongoing efforts to unravel the molecular complexities of this process hold the promise of improved diagnostic and prognostic tools, as well as the development of novel targeted therapies. The integration of advanced molecular diagnostics, personalized medicine, and innovative therapeutic approaches offers the hope of transforming the management of FS-DFSP and improving the outcomes for patients with this challenging disease. The path forward involves continued collaboration between basic scientists, translational researchers, and clinicians to bridge the gap between bench and bedside. By harnessing the power of cutting-edge technologies and innovative research strategies, we can strive to unravel the mysteries of fibrosarcomatous transformation and develop more effective strategies to combat this aggressive variant of DFSP.[11-13]

The critical importance of early and accurate diagnosis in the context of fibrosarcomatous dermatofibrosarcoma protuberans (FS-DFSP) cannot be overstated. The timely identification of this aggressive variant of DFSP is paramount in guiding

appropriate therapeutic decision-making and ultimately optimizing patient outcomes. The subtle and often deceptive clinical presentation of FS-DFSP, which can closely mimic that of conventional DFSP, poses a significant challenge to clinicians, frequently leading to delays in diagnosis and the initiation of treatment. The consequences of such delays can be profound, as the aggressive nature of FS-DFSP necessitates prompt and aggressive intervention to curtail its progression and improve patient survival. The clinical presentation of FS-DFSP can be remarkably similar to that of conventional DFSP, often manifesting as a slow-growing, painless, and indurated plaque or nodule on the skin. This clinical similarity can lead to a false sense of security, as clinicians may initially misinterpret the lesion as a benign or indolent process. The insidious nature of FS-DFSP's growth further contributes to the diagnostic challenge, as patients may not seek medical attention until the tumor has reached a considerable size or has caused significant functional impairment. The delay in diagnosis allows the tumor to progress unabated, potentially leading to local invasion, regional lymph node involvement, and distant metastasis. The importance of maintaining a high index of suspicion for FS-DFSP cannot be overemphasized. Clinicians should be particularly vigilant in patients with recurrent DFSP or those exhibiting atypical clinical or radiological features. The presence of rapid growth, pain, ulceration, or fixation to underlying structures should raise concerns for the possibility of fibrosarcomatous transformation. The integration of clinical acumen with appropriate diagnostic modalities is crucial in ensuring the timely and accurate identification of FS-DFSP. Histopathological examination remains the cornerstone of diagnosis in FS-DFSP. The definitive diagnosis hinges upon the identification of a high-grade sarcomatous component within the tumor, typically fibrosarcoma. The pathologist plays a pivotal role in meticulously examining the biopsy specimen, searching for the telltale signs of fibrosarcomatous transformation. These signs include increased cellularity, nuclear pleomorphism, atypical mitotic figures, and areas of necrosis. The accurate interpretation of these histopathological features is essential in distinguishing FS-DFSP from other spindle cell sarcomas, which may exhibit overlapping clinical and radiological characteristics. Immunohistochemical staining can serve as a valuable adjunct to histopathological examination in the diagnosis of FS-DFSP. The use of specific antibodies can help to highlight the expression of certain proteins that are characteristic of fibrosarcoma, such as vimentin, smooth muscle actin, and desmin. The integration of histopathological and immunohistochemical findings allows for a more confident diagnosis of FS-DFSP, guiding subsequent therapeutic decision-making. Recent advances in molecular diagnostics have opened new avenues for the earlier and more precise diagnosis of FS-DFSP. Next-generation sequencing (NGS) and gene expression profiling technologies enable the comprehensive analysis of the tumor's genetic and epigenetic landscape, providing insights into the molecular drivers of fibrosarcomatous transformation. The identification of specific genetic and epigenetic alterations associated with FS-DFSP may facilitate the development of non-invasive diagnostic tests, such as liquid biopsies, that can detect the presence of this aggressive variant at an earlier stage. Liquid biopsies, which involve the analysis of circulating tumor DNA or other biomarkers in the blood, offer the potential for minimally invasive and real-time monitoring of tumor dynamics. The detection of specific genetic or epigenetic alterations associated with FS-DFSP in the blood could serve as an early warning sign, prompting further investigation and timely intervention. The integration of liquid biopsies into the diagnostic algorithm for DFSP could revolutionize the management of this disease, enabling the identification of patients at high risk for fibrosarcomatous transformation and facilitating the implementation of preemptive therapeutic strategies. The timely diagnosis of FS-DFSP has a profound

impact on patient outcomes. Early detection allows for the prompt initiation of appropriate therapy, potentially preventing local invasion, regional lymph node involvement, and distant metastasis. The implementation of aggressive surgical resection with wide margins, coupled with adjuvant radiation therapy and systemic therapy, can significantly improve the chances of achieving long-term disease control and survival. Furthermore, early diagnosis enables the implementation of personalized medicine approaches, tailoring treatment strategies to the specific molecular profile of the tumor. The identification of targetable genetic alterations in FS-DFSP could lead to the development of novel targeted therapies that can specifically disrupt the signaling pathways driving tumor growth and metastasis. The integration of molecular diagnostics with personalized medicine holds the promise of transforming the treatment landscape for FS-DFSP, offering patients more effective and less toxic therapeutic options.[14,15]

The management of fibrosarcomatous dermatofibrosarcoma protuberans (FS-DFSP) necessitates a multifaceted and adaptable therapeutic approach that harnesses the strengths of various treatment modalities, including surgery, radiation therapy, and systemic therapy. The selection and sequencing of these modalities are guided by a multitude of factors, including the extent of the disease, the presence of metastatic spread, the patient's overall health status, and the evolving understanding of the tumor's molecular underpinnings. The goal of treatment is to achieve long-term disease control and improve patient survival while minimizing treatment-related morbidity. Wide local excision with the attainment of clear margins remains the cornerstone of treatment for localized FS-DFSP. The surgical approach aims to remove the macroscopic tumor burden while ensuring that no microscopic extensions of the tumor are left behind. The recommended margin width for excision varies depending on the location and depth of the tumor, but typically ranges from 2 to 4 cm. The achievement of clear margins is critical in reducing the risk of local recurrence, which remains a significant challenge even after adequate surgical resection. The surgical management of FS-DFSP can be technically demanding, particularly in cases where the tumor involves critical structures or has infiltrated into adjacent tissues. The expertise of a skilled surgical oncologist is essential in ensuring complete tumor removal while preserving functional and cosmetic outcomes. In some cases, reconstructive surgery may be necessary to restore the integrity and function of the affected area. Radiation therapy has emerged as a valuable adjuvant treatment modality in the management of FS-DFSP, particularly in scenarios where surgical margins are close or positive. The precise role of radiation therapy in FS-DFSP is still being defined, but it is generally recommended for patients with high-risk features, such as large tumor size, deep invasion, or positive margins. The rationale behind adjuvant radiation therapy is to eradicate any residual microscopic tumor cells that may have been left behind after surgery, thereby reducing the risk of local recurrence. The optimal radiation dose and fractionation schedule for FS-DFSP are areas of active investigation. Current recommendations suggest doses ranging from 50 to 60 Gy, delivered in daily fractions over several weeks. The delivery of radiation therapy can be tailored to the specific needs of the patient, taking into account the location and extent of the tumor, as well as the patient's overall health status. Technological advancements in radiation therapy, such as intensity-modulated radiation therapy (IMRT) and proton therapy, offer the potential for more precise targeting of the tumor while minimizing the exposure of surrounding healthy tissues to radiation. These advancements may lead to improved therapeutic outcomes and reduced treatment-related complications. Systemic therapy options for FS-DFSP are currently limited, but targeted therapies, such as imatinib, have shown promise in the treatment of advanced or metastatic disease. Imatinib, a tyrosine kinase inhibitor that

targets PDGFRB, has demonstrated efficacy in inducing tumor responses in a subset of patients with FS-DFSP. The molecular rationale for the use of imatinib stems from the frequent overexpression of PDGFRB in DFSP, including its fibrosarcomatous variant. The constitutive activation of PDGFRB drives tumor cell proliferation and survival, making it an attractive therapeutic target. Clinical trials have evaluated the efficacy of imatinib in patients with advanced or metastatic DFSP, including those with FS-DFSP. These trials have demonstrated that imatinib can induce objective tumor responses, including complete and partial responses, in a proportion of patients. However, the duration of response is often limited, and the development of resistance to imatinib remains a significant challenge. Ongoing research is focused on identifying mechanisms of resistance and developing strategies to overcome them. The combination of imatinib with other targeted therapies or conventional chemotherapy is also being explored as a means of enhancing its efficacy and durability of response. The role of immunotherapy in the management of FS-DFSP is an area of active exploration and holds great promise for the future. Immunotherapy harnesses the power of the immune system to recognize and eliminate cancer cells. Immune checkpoint inhibitors, a class of immunotherapy drugs that unleash the brakes on the immune system, have shown remarkable success in the treatment of various malignancies. Preliminary studies have suggested that immune checkpoint inhibitors may also have a role in the treatment of DFSP, including FS-DFSP. The rationale for the use of immune checkpoint inhibitors in FS-DFSP is based on the observation that these tumors often express immune checkpoint molecules, such as PD-L1, which can suppress the anti-tumor immune response. By blocking these immune checkpoints, immune checkpoint inhibitors can unleash the immune system to attack and destroy cancer cells. Early clinical trials have shown encouraging results with immune checkpoint inhibitors in patients with advanced DFSP, including those with FS-DFSP. However, further research is needed to define the optimal patient selection criteria and treatment regimens for immunotherapy in this setting. The management of FS-DFSP requires a multidisciplinary approach that involves collaboration among various specialists, including surgical oncologists, radiation oncologists, medical oncologists, pathologists, and radiologists. The expertise of each specialist is crucial in ensuring the accurate diagnosis, staging, and treatment of this complex disease. The multidisciplinary team works together to develop a personalized treatment plan for each patient, taking into account the individual's unique clinical and molecular characteristics. Regular follow-up and surveillance are essential in the management of FS-DFSP, as the risk of local recurrence and distant metastasis persists even after successful treatment. The multidisciplinary team plays a critical role in monitoring the patient's progress, detecting any signs of recurrence or metastasis early, and adjusting the treatment plan as needed. The long-term management of FS-DFSP requires a commitment to ongoing care and collaboration between the patient and the healthcare team.[16-18]

The presence of fibrosarcomatous transformation in dermatofibrosarcoma protuberans (FS-DFSP) carries significant prognostic implications, casting a shadow over the generally favorable outlook associated with conventional DFSP. The transition from a low-grade to a high-grade sarcoma heralds a shift towards a more aggressive clinical behavior, characterized by an increased propensity for local recurrence, distant metastasis, and a diminished overall survival rate. The grim reality of this transformation underscores the critical importance of early detection, accurate diagnosis, and the implementation of aggressive therapeutic strategies to mitigate its adverse impact on patient outcomes. The prognosis of FS-DFSP is undeniably less favorable compared to its conventional counterpart. The acquisition of a high-grade sarcomatous component within the tumor marks a turning point

in the disease's trajectory, signifying a heightened potential for local and distant spread. The 5-year survival rates for patients with FS-DFSP have been reported to range from 30% to 50%, a stark contrast to the near 100% 5-year survival rate observed in patients with localized DFSP. The sobering statistics associated with FS-DFSP highlight the urgent need for improved diagnostic and therapeutic approaches to combat this aggressive variant. Several factors have been identified as potential prognostic indicators in FS-DFSP, offering insights into the complex interplay of variables that influence patient outcomes. Tumor size, a readily measurable parameter, has been consistently associated with prognosis. Larger tumors tend to exhibit a more aggressive behavior, with a higher likelihood of local recurrence and distant metastasis. The depth of invasion, another crucial factor, reflects the extent to which the tumor has penetrated into the surrounding tissues. Deeper invasion is often associated with a greater risk of local recurrence and a poorer prognosis. The mitotic rate, a measure of the tumor's proliferative activity, serves as a surrogate marker for its aggressiveness. A higher mitotic rate indicates a more rapid cell division and growth, which is often associated with a greater propensity for invasion and metastasis. The presence of necrosis, or areas of dead tissue within the tumor, is another ominous sign, reflecting the tumor's outstripping of its blood supply and its aggressive growth pattern. The presence of necrosis has been linked to a poorer prognosis in FS-DFSP. The identification and validation of reliable prognostic biomarkers in FS-DFSP represent an area of active investigation. The development of such biomarkers would enable clinicians to more accurately predict the clinical course of the disease and tailor treatment strategies accordingly. Molecular markers, such as specific genetic mutations or alterations in gene expression patterns, hold great promise as potential prognostic indicators. The integration of molecular diagnostics with traditional clinical and pathological parameters could lead to the development of more refined prognostic models that can guide therapeutic decision-making and improve patient outcomes. The prognostic implications of FS-DFSP necessitate a nuanced and individualized approach to treatment. The selection of appropriate therapeutic strategies should be guided by a careful assessment of the patient's clinical and molecular profile, taking into account factors such as tumor size, depth of invasion, mitotic rate, and the presence of necrosis. The multidisciplinary management of FS-DFSP, encompassing surgery, radiation therapy, systemic therapy, and potentially immunotherapy, offers the best hope for achieving long-term disease control and improving patient survival. The aggressive nature of FS-DFSP often warrants the consideration of more intensive therapeutic approaches compared to conventional DFSP. Adjuvant radiation therapy may be recommended even in cases with microscopically negative margins, given the high risk of local recurrence. Systemic therapy, such as imatinib or other targeted agents, may be considered for patients with advanced or metastatic disease. The integration of immunotherapy into the treatment paradigm holds promise for enhancing the anti-tumor immune response and improving patient outcomes. The prognostic implications of FS-DFSP should be communicated to patients in a clear and compassionate manner. Open and honest discussions about the potential risks and benefits of different treatment options are essential in empowering patients to make informed decisions about their care. Shared decision-making, a collaborative process between the patient and the healthcare team, fosters a sense of autonomy and control, promoting patient satisfaction and adherence to treatment. The prognostic landscape of FS-DFSP is complex and multifaceted. The presence of fibrosarcomatous transformation heralds a shift towards a more aggressive clinical behavior and a less favorable prognosis. The identification and validation of reliable prognostic biomarkers, coupled with the development of novel therapeutic approaches, are crucial in improving the outcomes for patients with

this challenging disease. Continued research and innovation in this field offer the hope of transforming the management of FS-DFSP and providing patients with the best possible chance of long-term survival and quality of life.[19,20]

4. Conclusion

The case presented in this report underscores the challenges associated with recurrent DFSP that has undergone fibrosarcomatous transformation. The aggressive nature of this disease, coupled with the limitations of current therapeutic options, emphasizes the need for continued research and innovation in this field. The multidisciplinary management of FS-DFSP, encompassing surgery, radiation therapy, systemic therapy, and potentially immunotherapy, offers the best hope for improving patient outcomes. The development of novel diagnostic and prognostic biomarkers, as well as targeted therapies and immunotherapeutic approaches, represents a promising avenue for advancing the field and providing patients with this challenging disease with the best possible outcomes.

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