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Case Report

Tumefactive Fibroinflammatory Lesion: A Diagnostic Dilemma

Promil Jain[1], MD;
Rajeev Sen[1], MD;
Nisha Sharma[1], MD;
Shilpi Bhargava[1], MD;
Virender Singh[2], MDS

[1]Department of Pathology, Pt BDS PGIMS, University of Health Sciences, Rohtak, India;
[2]Department of Oral Pathology, PGIDS, University of Health Sciences, Rohtak, India

Correspondence:
Promil Jain, MD;
Department of Pathology,
Pt BD Sharma PGIMS, University of Health Sciences, Rohtak, 124001, India
Tel: +91 94 16312675
Email: jainpromil@gmail.com
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Abstract

Tumefactive fibroinflammatory lesions (TFLs) are rare idiopathic benign fibrosclerosing lesions that clinically simulate a malignancy. TFLs are seen more frequently in males between 10 and 74 years of age. The usual site of involvement is the head and neck region, but rarely the extremities may be involved. Coexisting fibrosclerotic processes have been reported including retroperitoneal fibrosis, sclerosing cholangitis, sclerosing mediastinal fibrosis, and orbital pseudotumors. The etiology of this poorly understood entity remains unknown. Possible suggestions include exaggerated responses or autoimmune reactions to any chronic infection. The clinical and radiological appearance of TFLs is that of malignancy, but histopathology reveals them to be a benign process broadly classified under non-neoplastic, fibroinflammatory proliferations. The treatment strategies for these lesions are not well defined and variable and include steroids, surgery, and radiotherapy either alone or in combination. TFLs, albeit not fatal, have a high recurrence rate; patients should, therefore, be kept on long-term follow-up. We describe a young female patient presenting with a rapidly developing cheek swelling, which was diagnosed histopathologically as a TFLs.

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Keywords ● Tumefactive fibroinflammatory lesion ● Sinus ● Neoplasms

What's Known

- Tumefactive fibroinflammatory lesions (TFILs) are rare benign lesions that are clinically aggressive and simulate a malignant process.
- Radiologically, TFILs are locally destructive but histologically, they are composed of mature sclerosing fibrous lesions of unknown etiology.

What's New

- In our patient, TFILs had grown to a very large size very fast, leading to clinico-radiological misdiagnosis of either fungal or malignant lesion.
- Extensive histopathological examination of such massive lesions is mandatory to reach the diagnosis.
- Only a few cases have been reported in the literature the world over.

Introduction

Tumefactive fibroinflammatory lesions (TFLs) constitute a rare idiopathic fibrosclerosing disorder. Clinically, TFLs mimic a malignant process due to their aggressive clinical behavior and locally destructive nature; however, histologically they are a benign lesion.[1] Depending on the site of occurrence, organ of origin, or predominant pathological features, TFLs have variably been termed "plasma cell granulomas", "xanthogranulomas", or "histiocytomas". Multiple synonyms are due to the rarity of these lesions and a lack of definite clinical criteria for classification. These are generally categorized under non-neoplastic, fibroinflammatory proliferations. The most common sites of involvement include the head and neck region, especially the sinonasal region and the neck region. Rarely the extremities may be affected.[2]

We introduce a case of this rare lesion presenting as a cheek mass with a view to contributing to the existing literature.

Case Presentation

Clinical Presentation

A 29-year-old woman was admitted with a history of a rapidly increasing swelling on the cheek of 1 month's duration. The patient initially felt a dull aching pain in the right upper back tooth region, which initially responded partially to a course of antibiotics and anti-inflammatory drugs. The intensity of the pain increased. On 2nd consultation, her 1st molar was extracted. The pain, however, was not relieved. After 2 days, she noticed swelling inside the mouth, which increased and grew large enough to appear on the cheek. The pain became throbbing and unbearable over the next few days, compelling her to seek medical attention in emergency services.

The patient was otherwise healthy without any relevant medical history. Her general physical examination was within normal limits. On local examination, a 3×2 cm firm, nodular, tender, noncompressible, nonfluctuant, and nonpulsatile swelling was noted on the right cheek. It extended superiorly to the infraorbital margin, medially to the alae of the nose, and laterally to 2 cm anterior to the pre-auricular region with an indistinct inferior margin. The overlying skin was normal in color and texture. No signs of paresthesia were elicited over the swelling (figure 1). Intra-oral examination revealed a firm and nodular swelling present on the right buccal vestibule extending from the 1st premolar to the 2nd molar region anteroposteriorly.

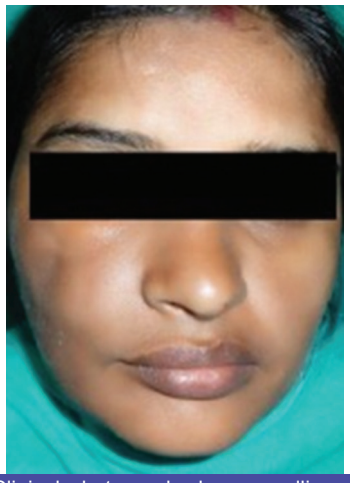

Figure 1: Clinical photograph shows swelling on the right cheek.

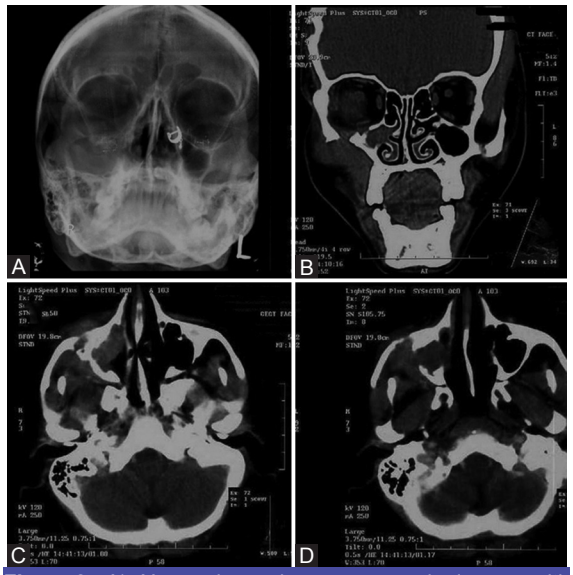

Figure 2: A) X-ray shows hazy paranasal sinuses with resorption of the bony walls. B), C), and D) Contrast-enhanced computed tomography face shows the mass on the right side.

Investigations

The patient's laboratory investigations were within normal limits. Radiography of the paranasal sinuses was reported as hazy along with resorption of the bony walls (figure 2A), hinting at the possibility of right maxillary sinusitis. Ultrasonography of the right cheek swelling revealed an irregular hypoechoic collection, 2.2×0.5 cm in size, seen in the muscle plain at the site of complaint, abutting the bone in the right cheek along with a hypoechoic lymph node, 2.3×1.1 cm in size. On contrast-enhanced computed tomography, an ill-defined and minimally enhancing soft-tissue mass, 3.4×3.1×2.4 cm in size, was seen involving the right infratemporal fossa and maxillary sinus with associated destruction of its lateral wall without any evidence of calcification/hemorrhage. Anterolaterally, the mass was causing destruction of the anterior root of the zygoma with extension into the premaxillary soft tissues. Superiorly, there was destruction of the floor of the orbit with an infratemporal extension, medially causing blockage of the osteomeatal complex and inferiorly destroying the maxillary bone (figures 2B, C, and D). The possibility of infective etiology of a fungal origin, without ruling out malignancy, was suggested.

Pathology

Biopsy from the mucosal aspect of the cheek was received with a clinical differential diagnosis of an infective lesion (of probably a fungal etiology), fibroma, and schwannoma. Histopathology of the biopsy revealed fibroadipose and fibrocollagenous tissue, showing dense chronic inflammation along with the formation of lymphoid follicles. Fungal stains were negative, and there was no evidence of granuloma or malignancy. Although the

swelling did not increase in size, a significant reduction in the swelling was not achieved and the patient continued to complain of severe pain. Within a week, repeat biopsy, labeled "soft tissue right buccal mucosa" and "right upper posterior teeth region", was submitted with special requisition again to rule out fungal infection. Microscopically, it revealed stratified squamous mucosa, submucosa, and deeper fibromuscular soft tissue enclosing the lobules of the minor salivary glands along with acute on chronic nonspecific inflammation. It was again negative for fungal infection and malignancy. Surgical intervention was done to remove the mass lesion. The intraoperative notes recorded included perforated posterior wall of the maxillary sinus. Intraoperative frozen section showed the destruction of the skeletal muscle, dense collagenization, and mild inflammation along with proliferating plump spindle cells. Soft tissues sent for direct immunofluorescence were negative for immune deposits.

Multiple biopsies, labelled "mass infratemporal space", "anterior border of the masseter muscle including the lesion", "anterior wall of the right maxillary antrum", and "other soft tissues from the zygomatic arch", were received. All the biopsies revealed almost similar histopathological features and consisted of necrotic antral mucosa, proliferating fibrous tissue, and bands of hyalinized collagen with dense chronic lymphoplasmacytic infiltrates with formation of lymphoid follicles and giant cells extending into the subcutaneous fat and septa along with varying stages of granulation tissue (figure 3). No cellular atypia or mitosis, typical or atypical, was seen even on extensive screening. Previous biopsies were also reviewed, which revealed a similar morphology. Based on the clinical and radiological findings (short history, large persistent swelling with evidence of bone destruction), special stains including PAS, GMS, and ZN stain (fungus, mycobacterium) were negative. Various differentials of reactive and neoplastic processes, which give similar appearances including nodular fasciitis, proliferative fasciitis inflammatory myofibroblastic tumors (IMTs), fibromatoses, pseudolymphomas, Kaposi sarcomas, fibrosarcomas, and lymphomas were kept.

Further extensive screening and immunohistochemical (IHC) stains with a review of literature were employed for a conclusive diagnosis. On IHC, spindle cells were positive for vimentin, SMA, with focal positivity for desmin and negative for cytokeratin, S-100, and ALK. CD34 was seen positive only in the

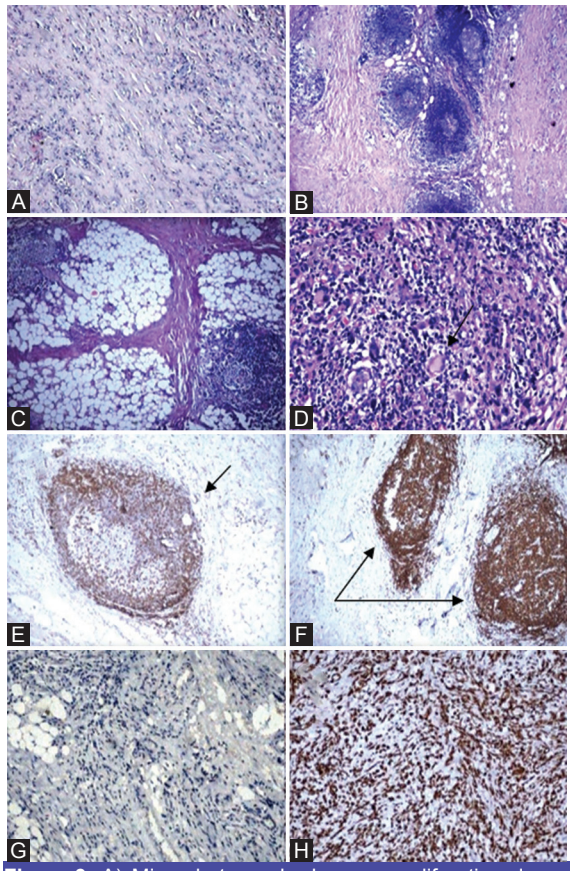

Figure 3: A) Microphotograph shows a proliferating dense fibrous tissue with collagen bands. B) Microphotograph shows a proliferating fibrous tissue with lymphoid follicles. C) Microphotograph shows findings of panniculitis with formation of lymphoid follicles. D) Microphotograph shows infiltration by lymphoplasmacytic cells with giant cell formation. E) Microphotograph shows lymphoid follicle, revealing CD5 positivity. F) Microphotograph shows lymphoid follicle, revealing CD20 positivity. G) Microphotograph shows ALK negativity. H) Microphotograph shows vimentin positivity in the spindle cells.

blood vessels in the granulation tissue. The lymphoid follicles revealed polyclonal positivity, showing the coexpression of CD3, CD5, and CD20 in different subpopulations of the same follicles (figure 3). Based on these IHC findings, the possibilities of the various differentials kept were excluded. A diagnosis of nodular fasciitis, proliferating fasciitis, and fibromatosis was ruled out due to dense inflammation, lack of a storiform pattern, and cellularity. The spindle cells lacked cytological atypia, mitosis, and nuclear hyperchromasia of sarcoma. Lymphoma was ruled out due to the polyclonal nature of the lymphoid cells on IHC. ALK negativity ruled out inflammatory fibroblastic tumor. Consequently, a diagnosis of a TFL was finally made.

The patient was started on steroid therapy after surgery. Complete imaging workup, including thoracic and abdominal imaging, was done to rule out other manifestations of idiopathic fibrosing conditions.

Discussion

The term "TFL" was first introduced by Wold and Weil and in 1983 to describe lesions of the head and neck that clinically simulate a malignant process in that they are locally invasive but histologically composed of mature sclerosing fibrous lesions interspersed with normal-appearing fibroblasts and lymphocytes.[3] Coexisting fibrosclerotic processes have been seen in 20% of cases including retroperitoneal fibrosis, sclerosing cholangitis, sclerosing mediastinal fibrosis, and orbital pseudotumors.[4] In medical literature, TFLs have been described under inflammatory pseudotumors.[2] To date, approximately only 35 cases have been reported in the literature. A wide age group is involved ranging from 10 to 74 years with a slight male predominance.[4] The etiology remains an enigma. The possible mechanism considered is an exaggerated immunological host tissue response to unidentified infectious agents, adjacent necrotic tissues, foreign bodies, or neoplasms or an autoimmune reaction to a previous viral infection. Smoking and chronic irritation by cocaine abuse have also been suggested as triggering factors for TFLs. Clinically, the patient usually presents with a hard and painful rapidly growing mass. Radiologically, it is seen as a locally destructive lesion simulating a malignancy. It is, however, on histopathological examination that the diagnosis becomes clear and malignancy is ruled out.[2]

Grossly, these lesions are firm and tannish-to-gray white and vary from being circumscribed to locally invasive. The histopathological features are of a benign lesion consisting of an admixture of fibrous tissue, collagen, and inflammatory cells associated with a giant cell reaction. TFLs can invade the adjacent soft tissues, muscles, and neurovascular structures and can erode the underlying bone with the involvement of the meninges and the brain.[5] Hence, any mass-forming lesion with any of these features should raise suspicion of malignancy. Our patient also presented with similar clinical, radiological, and histological findings. Even on extensive sampling, no malignancy or fungus/bacteria was detected. TFL-like lesions should be differentiated from more commonly encountered lesions of the head and neck like fibromatoses, nodular fasciitis, malignant fibrous histiocytomas, and fibrosarcomas. Fibromatoses are more cellular and lack the nest of inflammation seen in TFLs. Nodular fasciitis, seen in the head and neck, is a pseudosarcomatous self-limiting process which shows a prominent whorled or feathery cellular pattern lacking inflammatory infiltrates. Although TFLs are infiltrative, they lack the cellularity, cellular atypia, and mitotic activity seen in malignant fibrous histiocytomas and fibrosarcomas.[4] A differential diagnosis of TFLs also includes IMTs, which have been categorized under inflammatory pseudotumors. IMTs mainly occur in the lung, but they also have been seen in the head and neck area. Additionally, 50% of IMTs are ALK positive. However, in our patient, this entity was ruled out because ALK was negative. The diagnosis of TFLs is difficult.

The treatment of this rare condition is controversial. The treatment options include surgery, steroids, and radiation therapy either alone or in combination.[6] Some studies have shown steroids to be a better first-line treatment option, which may be followed by surgery and/or radiotherapy. Surgery is successful in surgically accessible sites, while radiation therapy is reserved for patients who do not respond to steroids or when the tumor extent limits surgical excision.[4,7] Our patient was put on steroids, followed by surgical excision, but she reported back after 6 months with similar complaints. She was subjected to reoperation, and histopathology showed similar findings.

Patients with TFLs have a high recurrence rate and higher chance of disease persistence.[8] Hence, these patients should be kept on regular follow-up and be assessed bearing in mind that TFLs may involve multiple body sites.

Conclusion

We introduced a rare case of TFL presenting as a cheek mass, which was biopsied for suspicion of malignancy because of its aggressive clinical presentation. Reaching a conclusive diagnosis was an uphill task. Such lesions should be kept a possibility while dealing with clinically aggressive, invasive lesions, especially in the head and neck region, and treated appropriately.

Conflict of Interest: None declared.

References

1. Binesh F, Taghipour SH, Navabii H. Tumefactive fibroinflammatory lesion: a rare aetiology for a neck mass in an old iranian man. BMJ Case Rep. 2011;2011. doi: 10.1136/bcr.12.2010.3572. PubMed PMID: 22692784; PubMed Central PMCID: PMC3128349.
2. Hoebers FJ, Ordonez BP, Irish J, Simpson RE, Yu E, O'Sullivan B. Progressive tumefactive fibroinflammatory lesion of the infratemporal

fossa treated by radiation therapy. Rare Tumors. 2012;4:32-6. doi: 10.4081/rt.2012.e12. PubMed PMID: 22532910; PubMed Central PMCID: PMC3325739.
3. Wold LE, Weiland LH. Tumefactive fibroinflammatory lesions of the head and neck. Am J Surg Pathol. 1983;7:477-82. PubMed PMID: 6614311.
4. Folpe AL. Soft-tissue tumors of the head and neck. In: Gnepp DR, editor. Diagnostic surgical pathology of the head and neck. 2nd ed. Philadelphia: Saunders, Elsevier; 2009. p. 647-728.
5. Holodny AI, Kirsch CF, Hameed M, Sclar G. Tumefactive fibroinflammatory lesion of the neck with progressive invasion of the meninges, skull base, orbit and brain. AJNR Am J Neuroradiol. 2001;22:876-9. PubMed PMID: 11337332.
6. Nirmala MJ, Parinitha SS, Ravikala VR. Idiopathic cervical fibrosis- a case report with review of literature. J Evol Med Dent Sci. 2014;3:56-9.
7. Fung K, Venkatesan VM, Heathcote JG, Lampe HB, Edmonds M. Tumefactive fibroinflammatory lesions of the head and neck: role of corticosteroids, radiotherapy, and surgery. J Otolaryngol. 2002;31:253-6. doi: 10.2310/7070.2002.21709. PubMed PMID: 12240766.
8. Hostalet F, Hellin D, Ruiz JA. Tumefactive fibroinflammatory lesion of the head and neck treated with steroids: a case report. Eur Arch Otorhinolaryngol. 2003;260:229-31. doi: 10.1007/s00405-002-0531-5. PubMed PMID: 12709810.