

# Tumor of follicular infundibulum—associated neoplasms



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## INTRODUCTION

Tumor of the follicular infundibulum (TFI) is a rare benign cutaneous adnexal neoplasm first described by Mehregan and Butler in 1961.<sup>1</sup> TFI most commonly presents as a solitary papule, plaque, or macule, on the head and neck region.<sup>2</sup> Clinical variants include multiple or eruptive forms.<sup>3</sup> Histopathologically, solitary lesions present as plate-like subepidermal proliferations of eosinophilic, pale-staining keratinocytes, creating a reticulated pattern.<sup>3,4</sup>

Many cases of TFI have been associated with other cutaneous lesions, stimulating discussions surrounding the histogenesis of TFI. Basal cell carcinoma (BCC) is the most commonly reported association, with varying rates of associated lesions seen in other reports.<sup>3</sup> Here, we present the case of a 69-year-old man with TFI and an associated dysplastic nevus.

## CASE REPORT

A 69-year-old man presented to the dermatology clinic for an annual skin check with a history of melanoma in situ and BCC on the right arm. On examination, there was a 4-mm atypical brown macule on the left upper back (Fig 1). The lesion was biopsied to rule out melanoma. On pathologic examination, hematoxylin-eosin–stained sections showed an atypical lentiginous junctional nevus (dysplastic nevus) (Fig 2, A). The atypical features included single melanocytic hyperplasia at the dermoepidermal junction, rete elongation and inter-rete bridging, lamellar fibroplasia, and a lymphocytic infiltrate. The melanocytes showed moderate cytologic atypia. Within the melanocytic proliferation, a

platelike proliferation of anastomosing strands of pale staining cells was noted to arise from the epidermis, consistent with a TFI (Fig 2, B). The lesion was diagnosed as a dysplastic nevus associated with a tumor of the follicular infundibulum.

## DISCUSSION

TFI is a rare benign neoplasm that usually presents as a solitary lesion on the head and neck region.<sup>5</sup> Less common clinical variants have been described, including multiple and eruptive forms, which are typically referred to as *infundibulomas*.<sup>6</sup> Infundibulomas are commonly found on the face, neck, and upper neck as well-demarcated hypopigmented lesions.<sup>5</sup> The solitary and multiple/eruptive variants of TFI present with similar histologic findings, namely, a proliferation of keratinocytes arranged in trabeculae and connected to the epidermis.<sup>7</sup> Although solitary variants tend to present in middle-age women, multiple and eruptive variants present in younger patients.<sup>5</sup>

TFI is often associated with other cutaneous lesions. These associations have generated discussion regarding the histogenesis of TFI. Some believe TFI differentiates toward the infundibulum, given the topography of tumor proliferation and glycogen in the tumor cells.<sup>1</sup> Others believe TFI differentiates toward the isthmus, given reports of sebaceous differentiation and trichilemmal differentiation.<sup>2</sup> With regard to their triggers, some argue TFI is a reactive process, whereas others believe TFI represents degeneration into BCC.<sup>2,8</sup> Some have postulated that TFI shares a common folliculosebaceous origin with other neoplasms, thus

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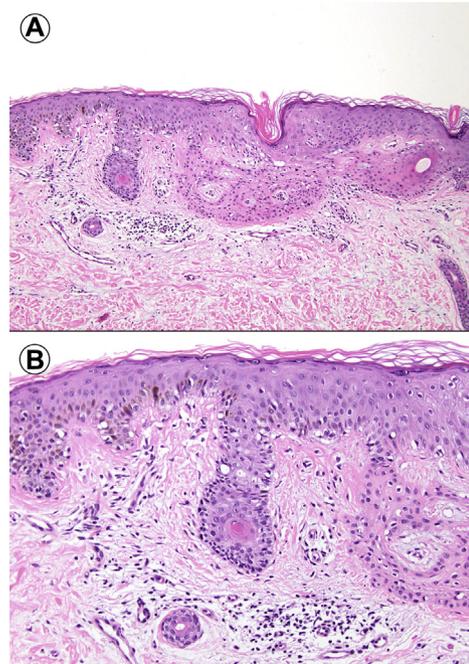


**Fig 1.** Dysplastic nevus with associated TIF. A 6-mm brown papule with a pink corner is present on the right upper back of this 69-year-old man with a history of melanoma and BCC.

explaining frequent associations with other cutaneous lesions.<sup>4</sup>

Since the discovery of TFI in 1961, there have been many accounts of associated neoplasms (Table I).<sup>9,13-17,19-21</sup> One of the first mentions of TFI-associated lesions was in 1989, by Kossard et al.<sup>6</sup> In studying eruptive infundibulomas, they found that the platelike epithelial architecture of TFI was seen in association with seborrheic keratoses and BCC.<sup>6</sup> They did, however, note that these lesions lacked the dense elastic brushwork of the follicular infundibulum.<sup>6</sup> In 1993, Ackerman et al<sup>22</sup> had not mentioned an association with BCC, but by 2001, they had observed this and attributed the association to chance.

In 1995, Cribier and Grosshans<sup>11</sup> reviewed 12 patients with TFI, and 3 of these patients had associated neoplasms. Two patients presented with TFI overlying a nevus sebaceus, and the third presented with TFI associated with a typical fibroma.<sup>11</sup> They proposed a classification system that included TFI and TFI changes associated with various tumors.<sup>11</sup> They found that the patient presenting with TFI associated with a typical fibroma



**Fig 2.** Biopsy of a lesion. **A**, A dysplastic nevus with single melanocytic hyperplasia at the dermoepidermal junction is seen with an associated tumor of the follicular infundibulum. **B**, Platelike proliferation of anastomosing strands of pale staining cells consistent with a tumor of the follicular infundibulum. (**A** and **B**, Hematoxylin-eosin stain; original magnifications: **A**,  $\times 4$ ; **B**,  $\times 20$ .)

lacked the elastic fiber network underlying the platelike proliferation of pale cells, suggesting that these were not classic TFI and, instead, TFI-like changes.<sup>11</sup> In 2001, Mahalingam et al<sup>18</sup> noted TFI associations with nevus sebaceus, BCC, and seborrheic keratosis.

After these early associations, a number of retrospective studies reviewed TFI-associated neoplasms, generating new hypotheses and challenging older postulations. In 2009, Weyers et al<sup>10</sup> reviewed 24 cases of TFI, 5 of which were associated with BCC. In 2 of these cases, there were foci showing continuity between TFI and BCC components, which they believed suggested a change in differentiation of the same type of cells, rather than the chance development of an entirely unrelated lesion, as Ackerman et al<sup>22</sup> had previously postulated.

During the same year, Abbas and Mahalingam<sup>2</sup> conducted an extensive retrospective study, reviewing cases of TFI between 1999 and 2008, with particular focus on histologic variants and associations, following 2 consecutive cases of TFI exhibiting atypia and desmoplasia. In this study, TFI was associated with cutaneous lesions in 25% of cases; specifically, TFI was found to be associated with

**Table I.** Summary of TFI-associated neoplasms in the literature

Associated neoplasm	Report	Frequency	
BCC	Baquerizo et al <sup>3</sup>	34/64 (53.12%) <sup>3</sup>	
	Alomari et al <sup>4</sup>	4/19 (21.05%) <sup>4</sup>	
	Lee et al <sup>9</sup>	1 (case report)	
	Weyers et al <sup>10</sup>	5/24 (20.83%) <sup>9</sup>	
	Abbas and Mahalingam <sup>2</sup>	7/53 (13.0%) <sup>2</sup>	
	Cribier and Grosshans <sup>11</sup>	1 (case report)	
	Inaloz et al <sup>12</sup>	1 (case report)	
	Macgregor et al <sup>13</sup>	1 (case report)	
	Schnitzler et al <sup>8</sup>	1 (case report)	
	Hutchinson et al <sup>14</sup>	4 (case reports)	
	Actinic keratosis	Baquerizo et al <sup>3</sup>	6/64 (9.38%) <sup>3</sup>
		Abbas and Mahalingam <sup>2</sup>	2/53 (3.77%) <sup>2</sup>
	Desmoplastic malignant melanoma	Abbas and Mahalingam <sup>2</sup>	1/53 (1.89%) <sup>2</sup>
Junctional melanocytic nevus	Abbas and Mahalingam <sup>2</sup>	1/53 (1.89%) <sup>2</sup>	
Desmoplastic trichilemmoma	Dore et al <sup>15</sup>	1 (case report)	
	Inaloz et al <sup>12</sup>	1 (case report)	
	Manonukul et al <sup>16</sup>	1 (case report)	
	Dore et al <sup>15</sup>	1 (case report)	
Trichoblastoma	Manonukul et al <sup>16</sup>	1 (case report)	
	Dore et al <sup>15</sup>	1 (case report)	
Epidermal Inclusion Cyst	Manonukul et al <sup>16</sup>	1 (case report)	
	Baquerizo et al <sup>3</sup>	2/64 (3.13%) <sup>3</sup>	
	Alomari et al <sup>4</sup>	1/19 (5.26%) <sup>4</sup>	
	Abbas and Mahalingam et al <sup>2</sup>	1/53 (1.89%) <sup>2</sup>	
	Cribier and Grosshans <sup>11</sup>	1 (case report)	
Nevus sebaceus	Dore et al <sup>15</sup>	1 (case report)	
	Alomari et al <sup>4</sup>	1/19 (5.26%) <sup>4</sup>	
	Cribier and Grosshans <sup>11</sup>	2 (case reports)	
	Schirren and Maciejewski <sup>17</sup>	2 (case reports)	
	Manonukul et al <sup>16</sup>	1 (case report)	
	Alomari et al <sup>4</sup>	10.53% (2/19) <sup>4</sup>	
Melanoma in situ	Alomari et al <sup>4</sup>	1/19 (5.26%) <sup>4</sup>	
Tinea versicolor	Alomari et al <sup>4</sup>	1/19 (5.26%) <sup>4</sup>	
Squamous cell carcinoma	Baquerizo et al <sup>3</sup>	2/64 (3.13%) <sup>3</sup>	
	Alomari et al <sup>4</sup>	3/19 (15.79%) <sup>4</sup>	
	Macgregor et al <sup>13</sup>	1 (case report)	
Lentigo maligna	Baquerizo et al <sup>3</sup>	2/64 (3.13%) <sup>3</sup>	
	Alomari et al <sup>4</sup>	3/19 (15.79%) <sup>4</sup>	
	Baquerizo et al <sup>3</sup>	2/64 (3.13%) <sup>3</sup>	
Intradermal nevus	Baquerizo et al <sup>3</sup>	2/64 (3.13%) <sup>3</sup>	
Syringoma	Baquerizo et al <sup>3</sup>	1/64 (3.13%) <sup>3</sup>	
Syringocystadenoma papilliferum	Dore et al <sup>15</sup>	1 (case report)	
	Mononukul et al <sup>16</sup>	1 (case report)	
	Alomari et al <sup>4</sup>	3/19 (15.79%) <sup>4</sup>	
Atypical junctional nevus	Alomari et al <sup>4</sup>	3/19 (15.79%) <sup>4</sup>	
Superficial epithelioma with sebaceous differentiation	Dempsey et al (current study)	1 (case report)	
	Lee et al <sup>9</sup>	1 (case report)	
	Mahalingam et al <sup>18</sup>	1 (case report)	
Mucoepidermoid carcinoma	Manonukul et al <sup>16</sup>	1 (case report)	
	Akasaka and Kon <sup>19</sup>	1 (case report)	
	Horn et al <sup>20</sup>	1 (case report)	
Hydrocystoma	Martin et al <sup>21</sup>	1 (case report)	
Adenosquamous carcinoma	Manonukul et al <sup>16</sup>	1 (case report)	

BCC, actinic keratosis, desmoplastic malignant melanoma, junctional melanocytic nevus, trichilemmoma, and epidermal inclusion cyst.<sup>2</sup> With the increased amount of associated lesions observed, they suggested that TFI may be a reactive process,

analogous to focal acantholytic dyskeratosis, epidermolytic hyperkeratosis, and cornoid lamellation.<sup>2</sup>

Similarly, in 2015, Baquerizo et al<sup>3</sup> performed a retrospective study, reviewing 67 cases spanning ten years. They found 23 of 64 lesions were associated

with other neoplasms, including BCC (12.5%), actinic keratosis (7.8%), epidermal cyst (3.13%), squamous cell carcinoma (3.13%), lentigo maligna (3.13%), intradermal nevus (3.13%), and syringoma (1.56%).<sup>3</sup> Compared with the highest rate of associated lesions in the studied performed by Abbas and Mahalingam,<sup>2</sup> this study presented an association up to 35%.<sup>3</sup> They also attributed these associations to a reactive process.<sup>3</sup> Our case showed a TFI that seemed to arise within the dysplastic nevus as opposed to adjacent to it, suggesting the TFI may be a reactive process in the setting of melanocytic proliferation.

Although many agree that TFI is a reactive process, Alomari et al<sup>4</sup> raised several points opposing the TFI-like reaction based on the unique features associated with TFI. Histopathologically, TFI was differentiated from BCC based on its unique staining pattern with a dense fiber network, not seen in BCC.<sup>4</sup> Additionally, they found that TFI lacks expression of Ber-EP4, in contrast to BCC, and that scattered Merkel cells are identified in TFI but are usually absent in BCC.<sup>4</sup> Based on this evidence, rather than deeming TFI a reactive process or a degeneration into BCC, as previously thought, they proposed that TFI may present with other lesions due to common folliculosebaceous origin.<sup>4</sup>

Alomari et al<sup>4</sup> also commented on reports of classic TFI merging with areas resembling BCC. This raises questions regarding the potential for malignant transformation, which is important clinically. The transformation has been described in 2 infundibulomas to date, notably in Schintzler's account of a 38-year-old woman with eruptive TFI, and thus, long-term follow-up is encouraged in these patients.<sup>12</sup>

Based on our review of the literature and findings in our case, many associated neoplasms have been reported, each adding to the complex pattern and histogenesis of TIF. Becoming cognizant of the array of TFI-associated lesions can potentially elucidate the etiology of TFI.

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