NON-INVASIVE FOLLICULAR THYROID NEOPLASM WITH PAPILLARY-LIKE NUCLEAR FEATURES (NIFTP) IN SOUTH AFRICA

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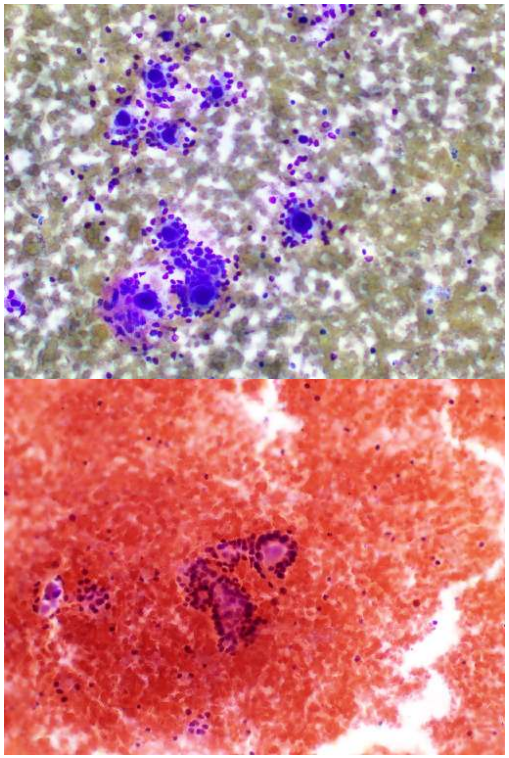
NON-INVASIVE FOLLICULAR THYROID NEOPLASM WITH PAPILLARY-LIKE NUCLEAR FEATURES (NIFTP)

- Non-invasive encapsulated follicular variant of papillary thyroid carcinoma has recently been reclassified into non invasive thyroid follicular neoplasm with papillary-like nuclear features (NIFTP)
- Goal: Promote more conservative management of these tumours including less extensive surgery and spare patients the psychological burden of a cancer diagnosis

USUAL MANAGEMENT OF PAPILLARY THYROID CARCINOMA

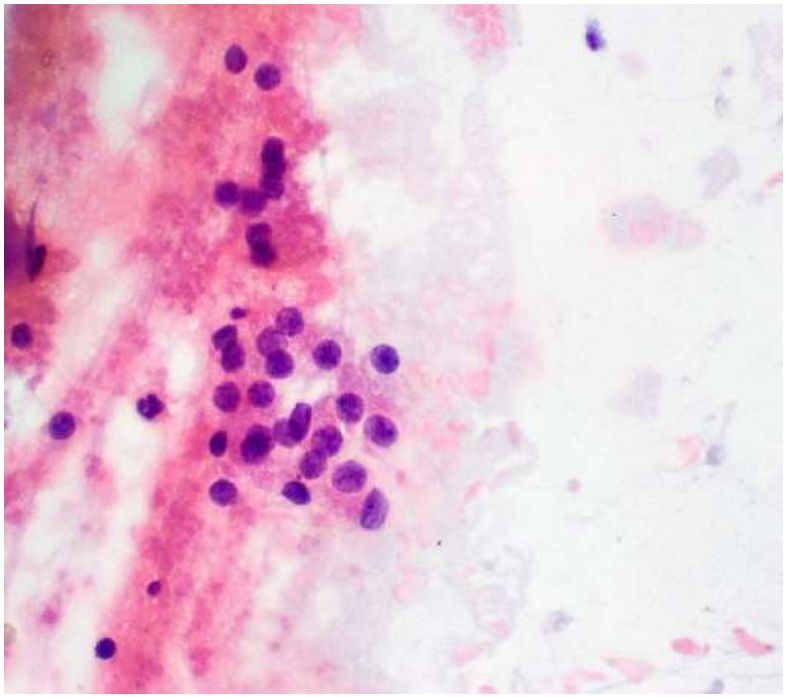
- PTC is generally managed by total thyroidectomy, central neck dissection and post operative radioactive Iodine
- Complications associated with this treatment regimen relate to
- 1. Hypothyroidism
- 2. Radioactive Iodine – salivary gland dysfunction and development of secondary malignancies

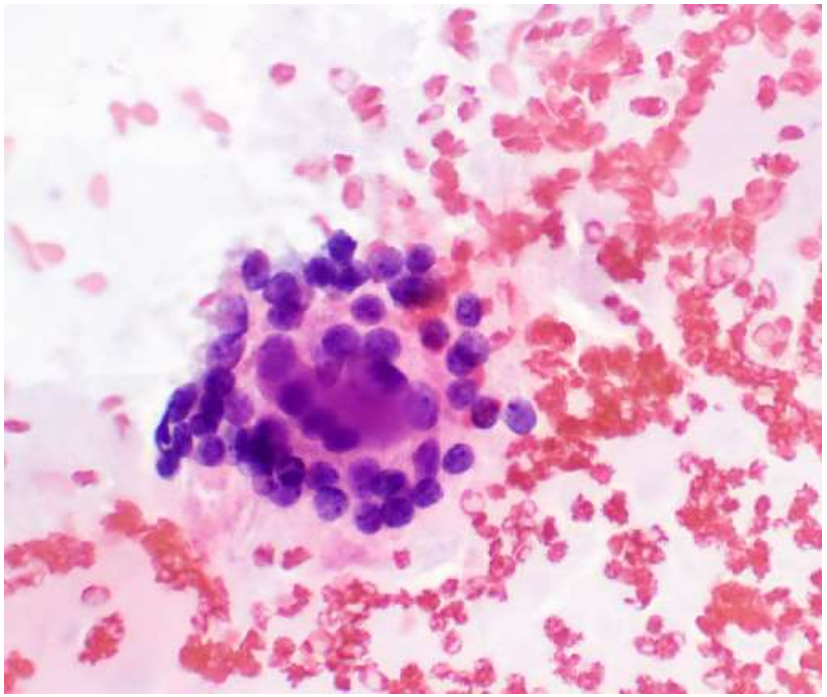
CASE STUDY



- 49F
- 5cm right thyroid mass present for 6 years.
- RVD+, CD4: 391.
- Thyroid function tests and thyroid scan results not available.

CASE STUDY





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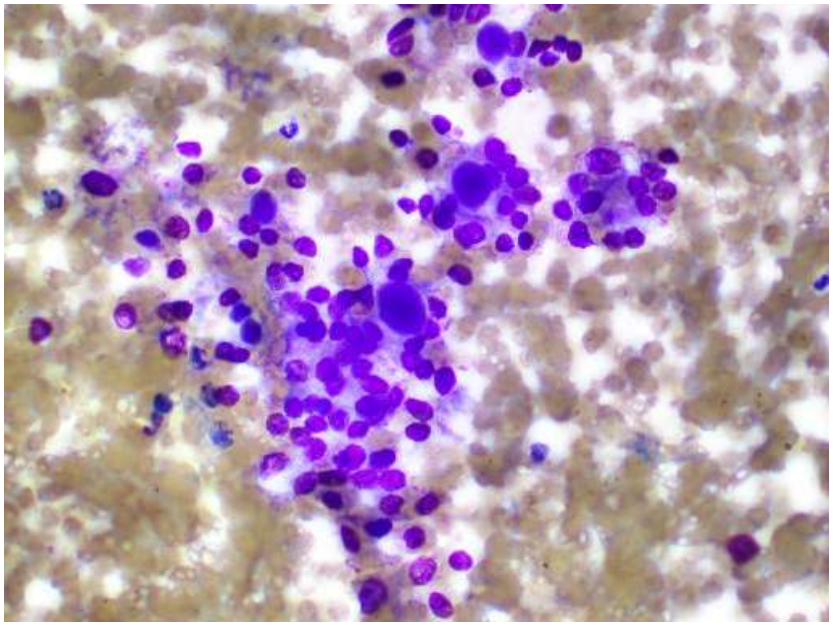

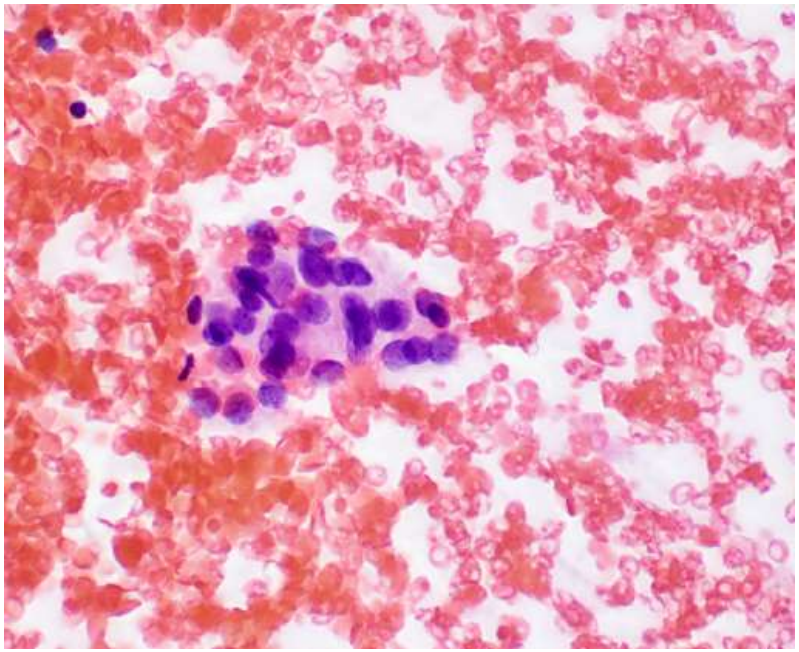

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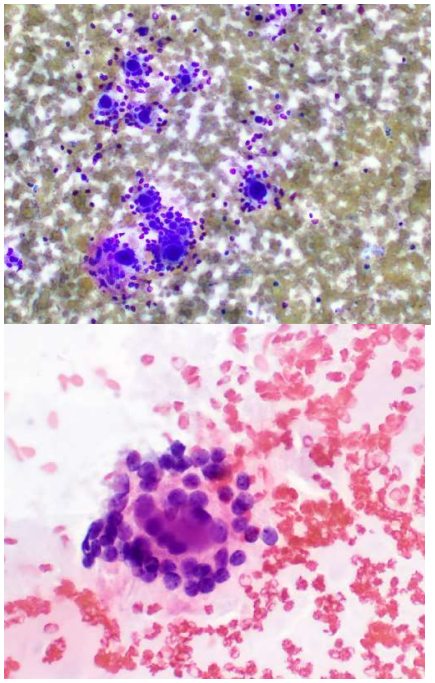


- Microfollicular pattern throughout
- Microfollicles with inspissated colloid
- Finely granular chromatin +- small nucleoli
- No intranuclear "holes"
- Very **focal** nuclear pallor and grooves
- **Follicular neoplasm**
- **Lobectomy recommended.**

CASE STUDY

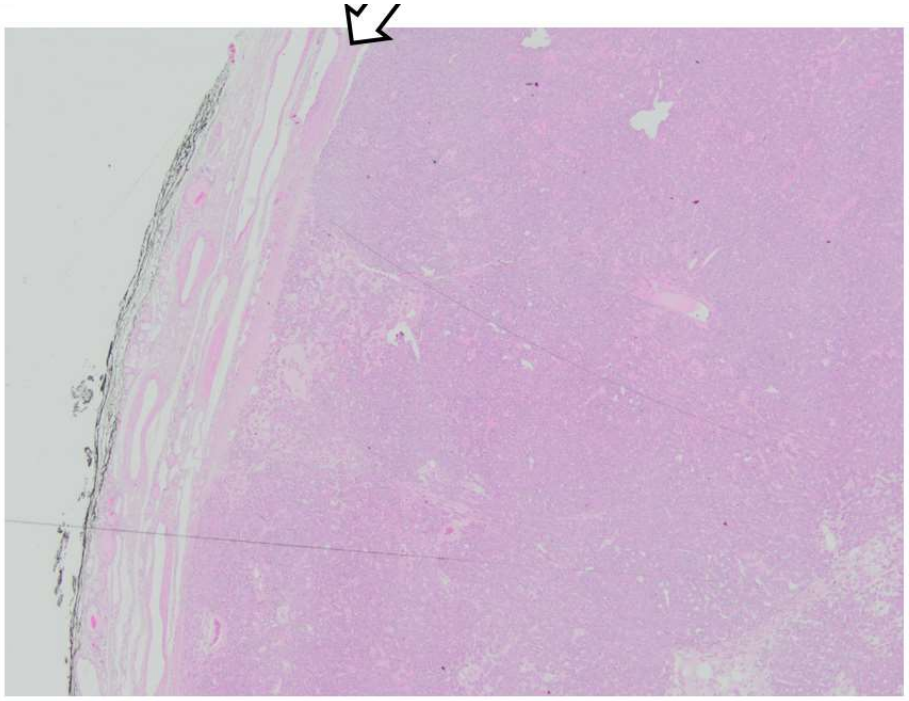
- Thyroid lobe with a solitary encapsulated nodule. The capsule varies from thin to thick in areas. The tumour has a homogenous cream coloured cut surface with areas of haemorrhage noted (arrow).

CASE STUDY

H&E 20x

Low power view of the neoplasm with an intact capsule at the periphery. There is no necrosis.

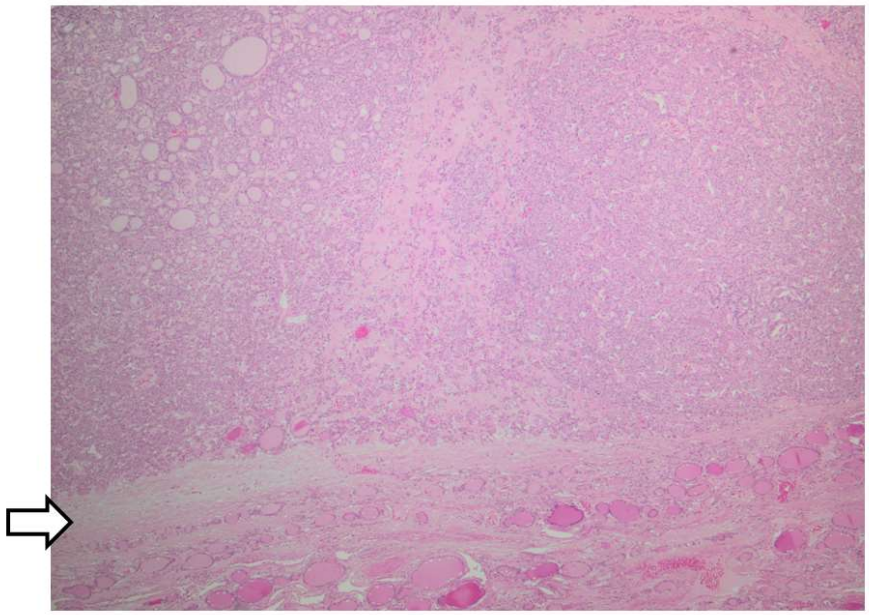
There is a lack of capsular invasion or lymphovascular invasion. (Entire capsule was processed and examined prior to making the diagnosis)



H&E 40x

Higher power view demonstrating the neoplasm (top) with a follicular architecture. The capsule with the adjacent normal thyroid parenchyma is evident at the bottom of the field.

There is no papillary, solid or trabecular growth patterns. There was less than 30% insular areas.

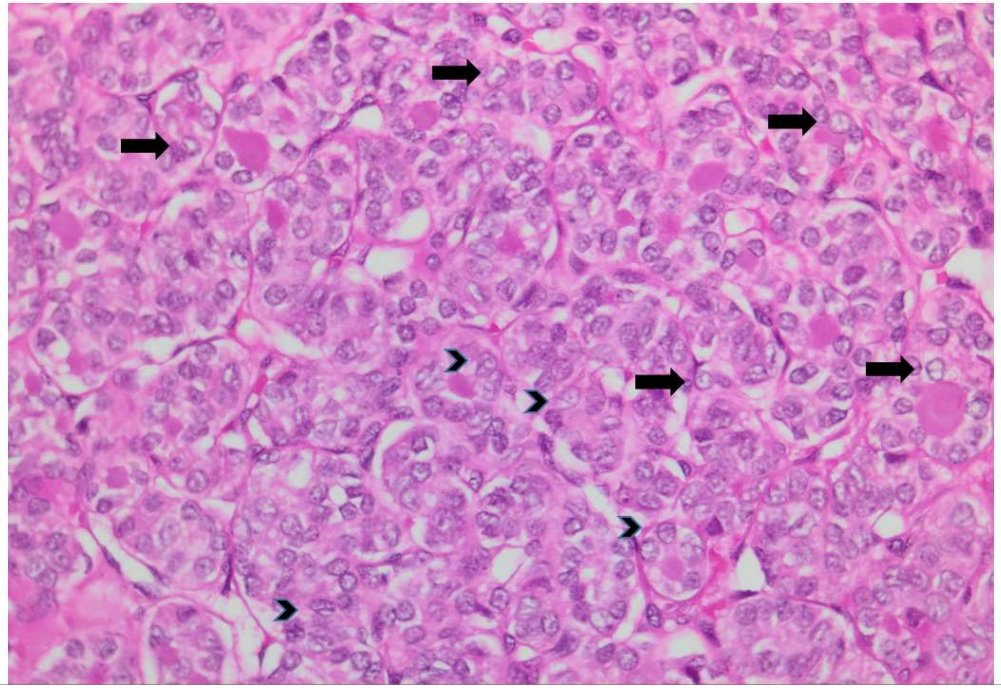


H&E 400x

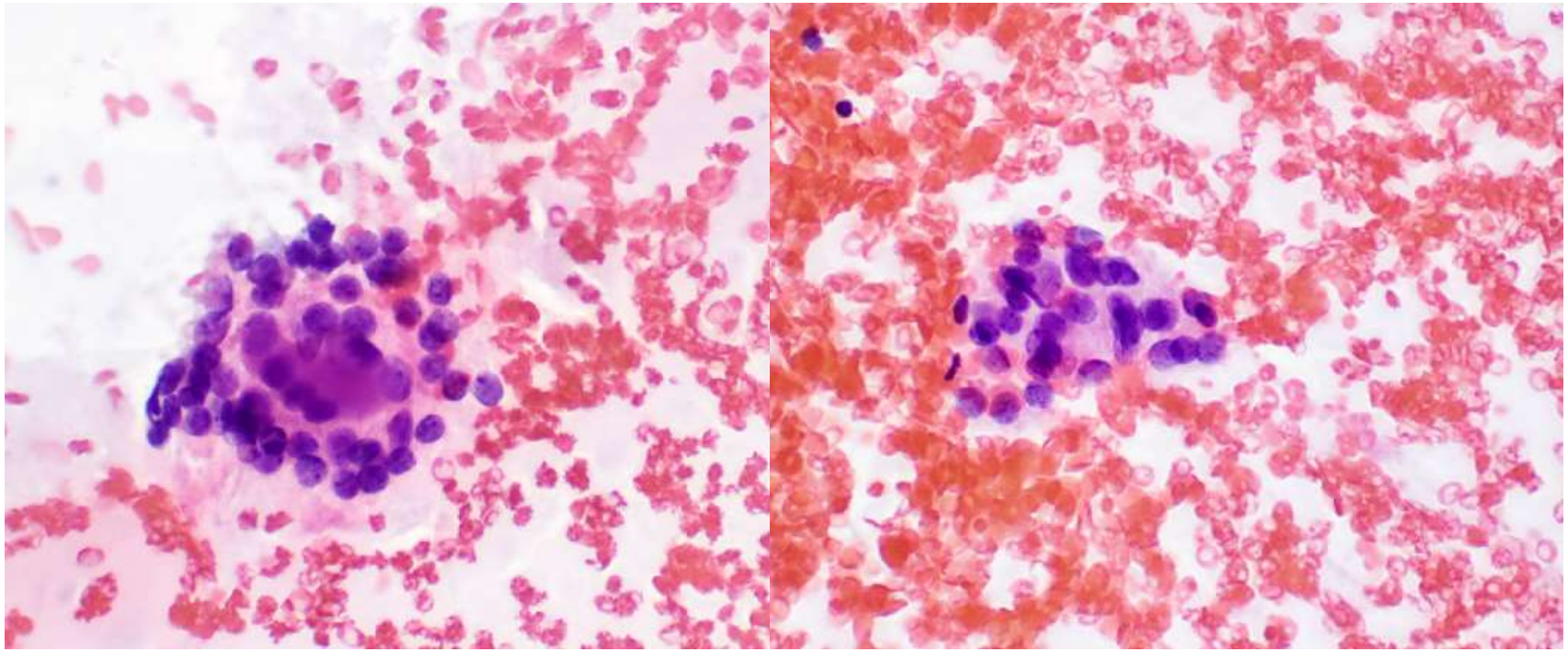
High power view demonstrating follicles lined by cells showing crowding and nuclear overlapping. In this field numerous nuclear grooves are present. Focally, chromatin clearing and margination is also present.

Nuclear groove (arrow head)

Chromatin clearing (arrow)



REVIEW OF CYTOLOGY



NIFTP

- **Histologic diagnosis:**
- Encapsulation or circumscription (no capsular/ vascular invasion)
- Follicular growth pattern (<1%) papillae.
- Nuclear features of PTC.
- If solid, trabecular or insular patterns seen; these in total should be less than 30% of the total tumor volume.
- No psammoma bodies
- No tumour necrosis (not associated with FNA) nor increased mitoses (at least 3 per 10 HPF)
- No *BRAF*^{V600E} mutations
- No distant metastasis
- In order to ensure that these inclusion and exclusion criteria are met, the tumour must be sampled extensively, with the entire capsule/periphery submitted in all cases

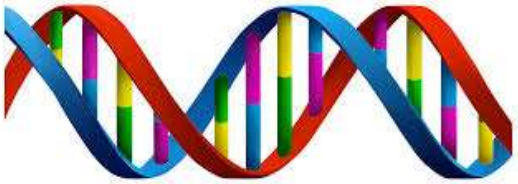
NIFTP CYTOPATHOLOGY

- Cellular smears
- Microfollicles (no papillae).
- Focal nuclear features of PTC: grooves, pallor
- Nuclear inclusions infrequent/ absent.
- +- Colloid

- Reporting option: Although the architecture suggests a follicular neoplasm (or another diagnostic category), some nuclear features raise the possibility of an invasive FVPTC or its indolent equivalent NIFTP; definitive diagnosis not possible cytologically.

NIFTP: MOLECULAR

- Frequent RAS mutations.
- Rarely BRAF K601E mutation
- Rarely gene rearrangements in PPARG
- Molecular profile similar to follicular adenoma/carcinoma



NIFTP CYTOLOGY

- Most NIFTP cases are placed in the Bethesda categories:
  - Follicular neoplasm (FN)
  - Suspicious for follicular (SFN)
  - Atypia of unknown significance (AUS) / follicular lesion of unknown significance (FLUS)
  - Suspicious for malignancy

- **Maletta et al, Human Pathology, 2016:**

Blind review of cytology from histologically-proved NIFTP:

- Follicular neoplasm 56%
- Suspicious for malignancy 27%
- AUS/FLUS 15%
- Malignant 2%

PM2

CYTOPATHOLOGY OF NIFTP

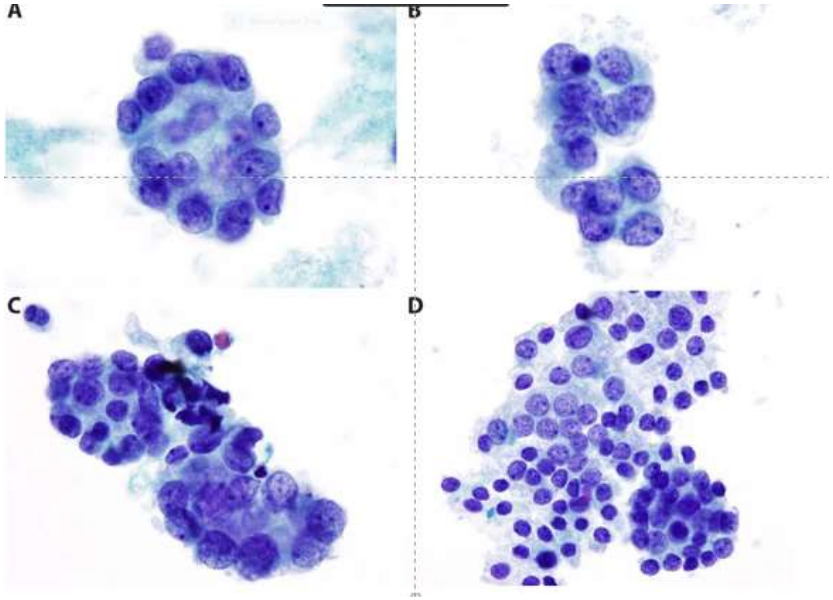
PM4

Mito et al, Cancer Cytopathology, 2017

- Made the criteria for PTC more stringent: Nuclear features of PTC + at least one of the following- frequent intranuclear holes (> 3), papillae, psammoma bodies.

- Explanatory notes in a certain subset of SFN or suspicious for malignancy suggesting possibility of NIFTP

Examined effect of this after 1 year of implementation



Slide 17

PM2 Pam Michelow, 4/23/2019

PM4 get the legends from the manuscript
Pam Michelow, 4/23/2019

CYTOPATHOLOGY OF NIFTP

Mito et al, Cancer Cytopathology, 2017

- No reduction in use of malignant category- most PTCs recognised as such.
- Minimal changes in proportions of other Bethesda thyroid categories.
- Most NIFTPs are recognised as being abnormal and placed in an indeterminate Bethesda category.
- 21% of NIFTP prospectively recognised.
- Using more stringent criteria for PTC does not change sensitivity of thyroid FNA and potentially **minimises** placing NIFTP in a malignant category.

REMOVING NIFTP ALTERS MALIGNANT RISK OF TBSRTC CATEGORIES

- Weihong et al, Sept 2017. Implementing noninvasive thyroid neoplasm with papillary-like nuclear features (NIFTP) may potentially impact the risk of malignancy for thyroid nodules categorized as ***AUS/FLUS*** and ***FN/SFN***.

COMPARISON OF ROM BEFORE AND AFTER EXCLUDING NIFTP FROM MALIGNANT CATEGORIZATION

TBSRTC Category	ROM before (%)	ROM after (%)	Absolute ROM decrease (%)	Relative ROM decrease (%)
ND	9,8	9,8	0	0
Benign	5,6	4,4	1,2	21,4
FLUS	12,8	9,5	3,3	**25,8**
SFN	26,5	20,6	5,9	**22,3**
SFM	81,4	79,1	2,3	2,8
Malignant	97,7	97,1	0,6	0,6

RELATIVE ROM DECREASE IN DIFFERENT STUDIES

Studies	Cases with surgical follow up	PTC – histologically proven %	Cases classified as NIFTP	ND %	Benign %	FLUS %	SFN %	SFM %	Malignant %
Strickland	655	304 (46,4)	72 (23.7)	10	59	45	18	48	5
Fanquin	1827	756 (41.4)	173 (22.8)	5,5	37,6	43,6	45,5	28,3	3,3
Canberk	1886	341 (18.1)	94 (27.5)	50	14	33	66	33	11,2
Layfield	315	-	-	0	33,6	13,2	11,3	20,5	12,8
Weihong	908	252	17	0	21,4	25,8	22,3	2,8	0,6

NIFTP MANAGEMENT

- Lobectomy with no post op radiation
- Long-term follow up studies show no risk of recurrence and or metastatic disease in different series

NIFTP IN JOHANNESBURG, SOUTH AFRICA

- A 3 year audit of thyroid fine needle specimens at our Cytology Unit was conducted. A search of our database for all thyroid cases from January 2015 to December 2017 was performed.
- A total of 4000 cases of thyroid FNAs were retrieved.
- Inadequate 23%
- Benign 60%
- AUS/FLUS 8%: NOS 5% and cannot exclude malignancy 3%
- Suspicious for follicular/Hürthle cell neoplasm 4%
- Suspicious for malignancy 2%
- Malignant 2%.
- Only two cases of NIFTP were diagnosed histologically in the time period. One met the morphologic criteria to be categorised as NIFTP both cytologically and histologically.
- Total of 5 cases of NIFTP were diagnosed in our circuit in the study period. 1 histologically confirmed case had no prior cytology. 2 cases were originally diagnosed as NIFTP on histology which behaved in an aggressive manner clinically. Review of both cases revealed areas of invasion. Diagnoses subsequently amended to invasive follicular variant of PTC. All 3 cases excluded from the current study.

NIFTP JOHANNESBURG

- Different patient demographics in the public health sector in Johannesburg?
  - Patients usually present with thyroid nodules 4cm in size and advanced thyroid disease. Often much larger nodule size
  - Rate of FV PTC about 7/10 PTCs
  - Less diagnosis of thyroid nodules as incidental findings.
- Histopathologists at our institution are aware of NIFTP as an entity but it is not a diagnosis that is frequently encountered: are they not making the diagnosis at present?
- Even though NIFTP is infrequently encountered at present, clinicians and pathologists have to be aware of this entity as it can significantly alter patient management where more conservative management may be warranted.

USUAL DAY AT FNA CLINIC!