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ABSTRACT

Background: The prevalence of tuberculosis (TB) in Korean children has decreased due to universal BCG vaccination and the national TB elimination project. However, exposure to TB in children has been consistently reported. There have been few reports of TB exposure in the pediatric hematology-oncology ward.

Methods: A mother of a pediatric cancer patient was diagnosed with active TB with a cavity. Contact investigation was performed on patients, their parents, and healthcare workers who were exposed to the index case. The criteria for close contact were exposure in the same space with the index patient for more than 8 hours continuously or a total of 40 hours in case of multiple exposures. The initial assessment was performed as soon as the index case was identified. The second evaluation was conducted 8–10 weeks after the initial exposure. Both tuberculin skin test (TST), TB Specific Interferon-Gamma (T-SPOT) tests, and chest radiography were used in immunocompromised pediatric patients. For immunocompetent adults, the QuantiFERON-TB Gold (QFT-G) test and chest radiography were performed.

Results: Total 23 patients and 29 parents were exposed. The median exposure duration of patients was 3 days (1–8 days). The initial evaluation did not detect TB infection in pediatric patients. However, at the second evaluation, five patients (17.4%) were diagnosed with latent TB infection (LTBI, three with positive TST and two with positive T-SPOT), and two patients (8.7 %) were diagnosed with active TB infection (lymphadenitis and pulmonary TB). Among the 29 parents, 11 individuals (37.9%) were diagnosed with LTBI at the initial evaluation, which was considered as preexisting LTBI before this exposure. No additional case of TB infection was identified in the second evaluation. Among exposed 24 healthcare workers, two (9.1%) were eventually confirmed as newly diagnosed LTBI.

Conclusion: TB exposure in pediatric hematology-oncology ward and outpatient chemotherapy clinic caused active TB or LTBI cases with an attack rate of 26% in children. The high LTBI rate, up to 38% among parents even before this exposure, needs further intervention such as routine LTBI evaluation and treatment for families of pediatric cancer patients to prevent a similar event.

BACKGROUND

- In 2021, 18,335 patients were newly diagnosed TB in Korea
- Foreigner: 1,242 (5.4%), MDR TB 371 (0.3%), XDR TB 4 (0.02%)
- Pediatric patients
 - 0-4y: 5 (0.3), 5-9 y: 6 (0.3), 10-14y: 26 (1.1), 15-19y: 155 (6.5) (/100,000)
- Contacts with latent tuberculosis infection (%)
 - ≤ 9 years 17.9%, 10-19 years: 6.3%
- Risk of TB with hematologic malignancies
 - 2-40 times higher that of general population

OBJECT

- To identify and initiate treatment of secondary cases of active TB disease or latent TB infection.

METHODS

- Subjects of study**
 - Contacts within 3 months before the collection date of the 1st positive AFB smear result or the symptom onset date (whichever is earlier)
 - Contacts who shared the same space ≥ 8 hours/ day or ≥ 40 hours in total
- Contact investigation strategy**
 - Pediatric cancer patients**
 - CXR, TST and/or T-SPOT (2 times with 8-10 weeks interval)
 - Preemptive treatment: High risk patients (hematopoietic cell transplantation recipients, ≤ 2years-of age) were pre-treated with isoniazid
 - Adults (parents of patients):** CXR, QuantiFERON-TB Gold (QFT-G) 2 times
 - Healthcare workers:** one time at 8~10 weeks after exposure in those who has previous QFT-G result within 6 months

RESULTS

1. Exposure by index patient (initial event)

- Index patient:** Female, Patient's mother
 - Symptoms: cough, hemoptysis (May 13, 2019)
 - Diagnosis: active tuberculosis (May 15, 2019)
 - Chest CT: **Cavity + pulmonary TB**,
 - TB characteristics: **AFB stain +, PCR +, all sensitive TB**
- Exposure time**
 - Admission (April 05 ~ 14, 2019) for 10 days, (May 05 ~ 06, 2019) for 2 days
 - Outpatient treatment center visit: (May 07 ~ May 1 0, 2019) for 4 days
 - Over 3hours OPD visit: 2 days
- Contacts who share the same space ≥ 8 hrs/day or ≥ 40 hours**
 - Hemato-oncology patients 23, Parents 29, Healthcare workers 24

2.1. Outcomes of exposed pediatric cancer patients

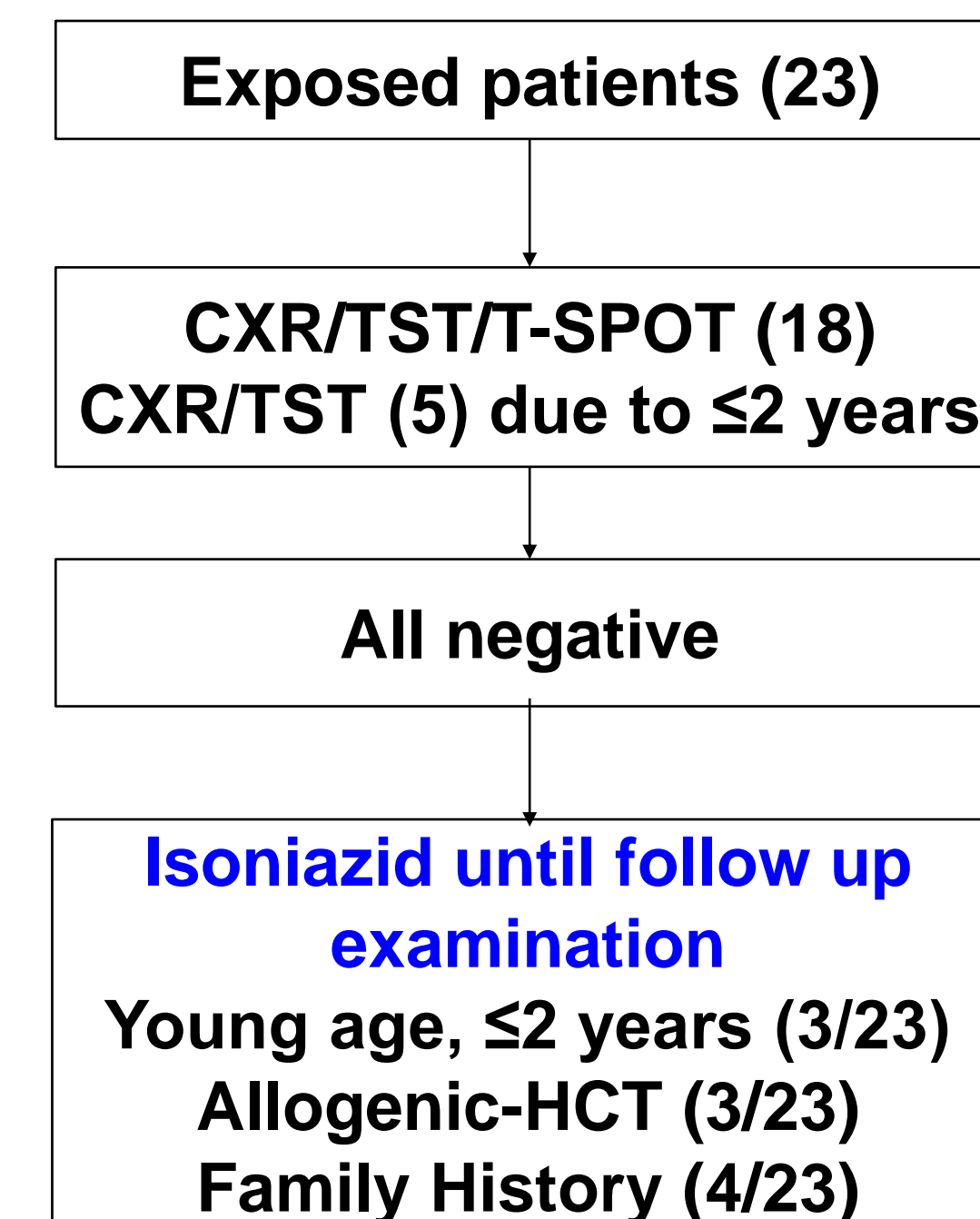


Fig 1. Evaluation of exposed patient (Initial examination)

Table 1. Characteristics of exposed pediatric patients

Characteristics	N (%)
Sex (male)	14 (60.9)
Age (years, median)	11 (6 mos-26 yrs)
≤ 2 years age	3 (13.0)
Underlying disease	
Solid tumor	14 (60.9)
Hematologic malignancy	9 (39.1)
Pre-exposure treatment	
Chemo tx	17 (73.9)
Allogenic-HCT	3 (13.0)
Exposure (days)	3 (1-8 days)
1-2 days	9 (39.1)
3-7 days	13 (56.5)
≥ 8 days	1 (4.3)

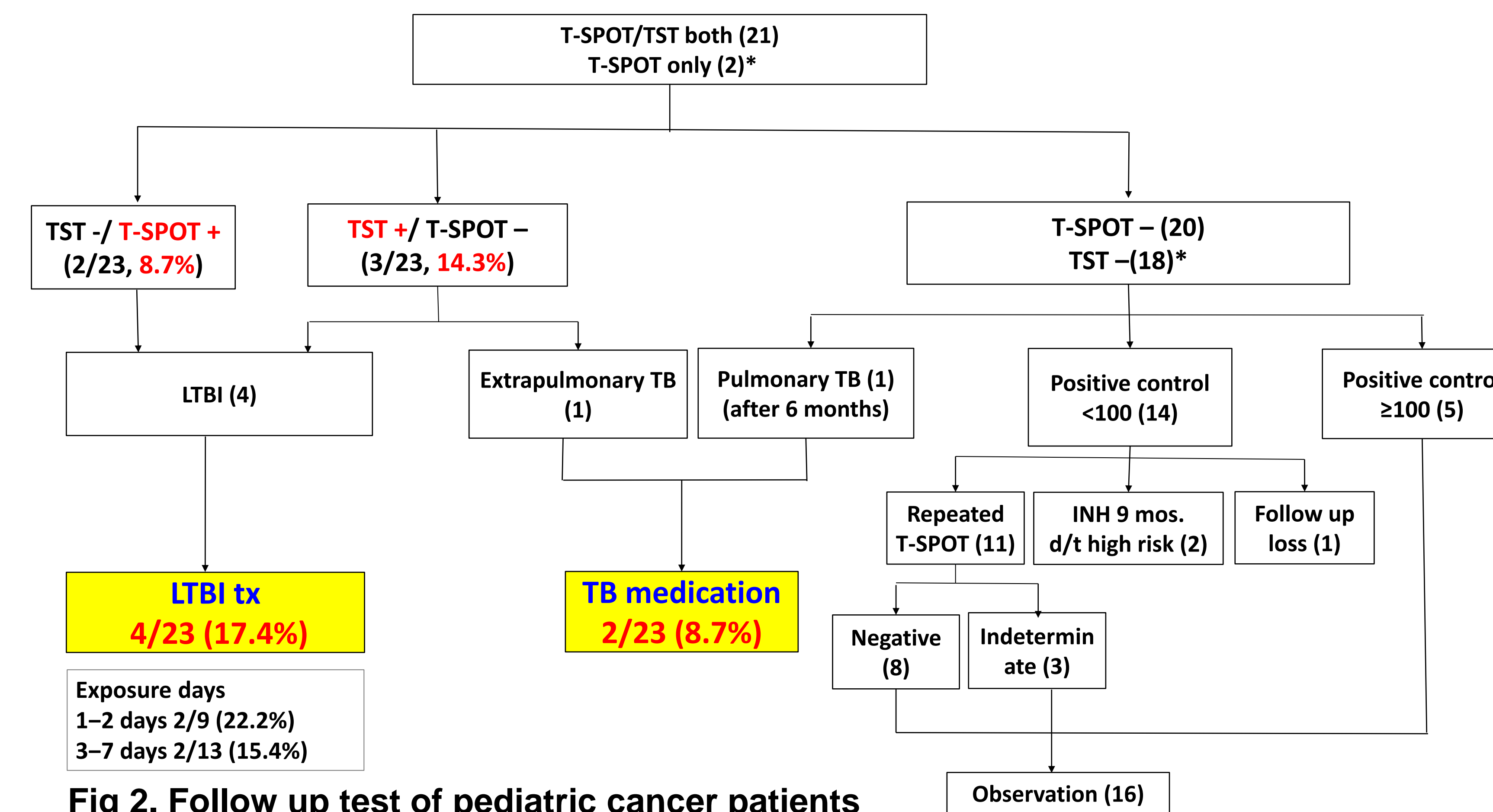


Fig 2. Follow up test of pediatric cancer patients

* Patients with over 18 years-age were not done TST, TST: Tuberculin skin test, T-SPOT: TB Specific Interferon-Gamma, INH: Isoniazid

2.2. Outcomes of exposed parents of patients

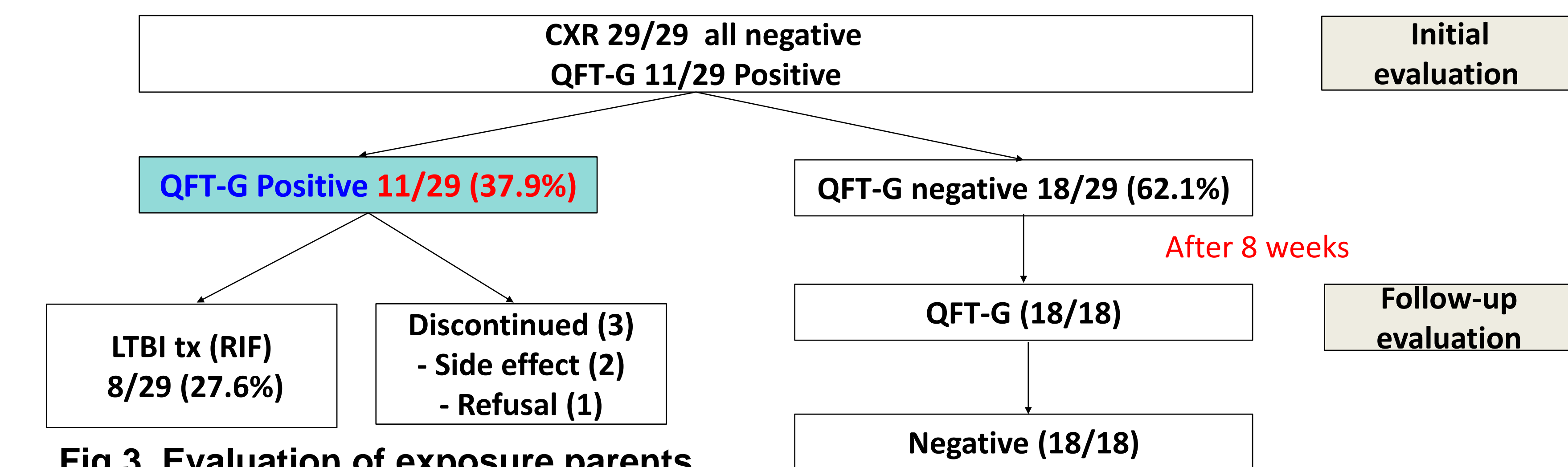


Fig 3. Evaluation of exposure parents

CXR: Chest x-ray, QFT-G: QuantiFERON-TB Gold

2.3. Outcomes of exposed healthcare workers

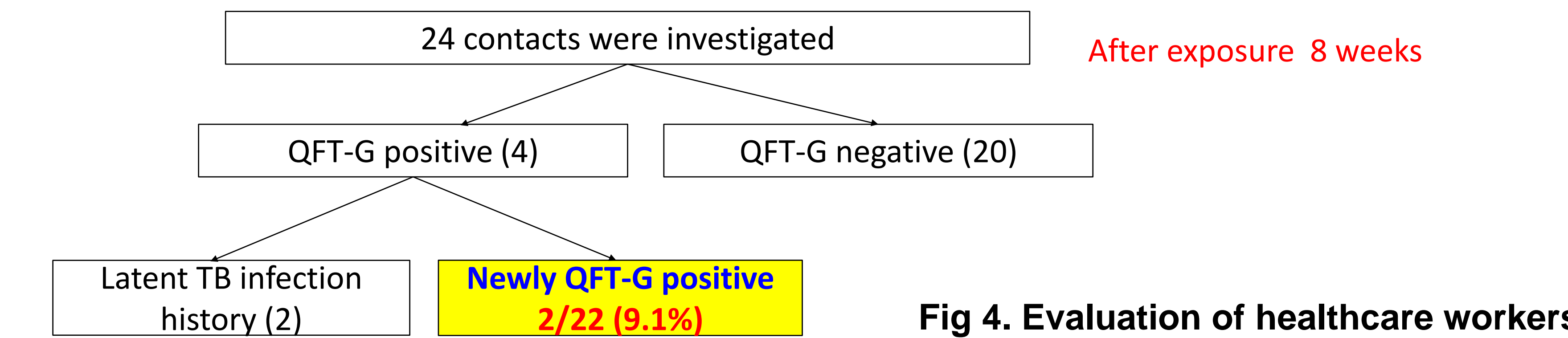


Fig 4. Evaluation of healthcare workers

3. Patients with TB or latent TB infection

Table 2. Characteristics of patients with tuberculosis or latent tuberculosis infection

Sex	Age (yr)	Diagnosis	Exposure days	Family hx	Underlying disease	Imaging	Medication
M	5	Extrapulmonary TB	2	-	Wilms' tumor	bilateral hilar LNE	1 yr (RIF 6mos)
F	18	Pulmonary TB	2	+ Father (LTBI)	Medulloblastoma	(6 m CT) peri bronchial nodular consolidation	1 m HERZ (discontinued d/t HCT)
F	8	LTBI	1	-	Klippel-Trenaunay-Weber SD	Normal	9 mos INH
F	7	LTBI	2	+ Both (LTBI)	Neuroblastoma	Normal	9 mos INH
F	13 mos	LTBI	4	-	Malignant neoplasm of vagina	Normal	9 mos INH
M	9	LTBI	3	+ Mother (LTBI)	Neuroblastoma	Normal	8 mos INH (d/c chemo tx)

SUMMARY

- Among 23 exposed pediatric patients, **26.1%** of total exposed pediatric patients were diagnosed with LTBI or TB; **17.4% (4/23)** of LTBI and **8.7% (2/23)** of TB were diagnosed
- Among exposed patients' parents, **37.9% (11/29)** already had LTBI at initial evaluation immediately after the exposure and none were newly diagnosed with LTBI during follow-up.
- Among exposed health care providers, **9.1% (2/22)** were newly diagnosed with LTBI.

CONCLUSION

- Exposure to an active TB case in a cancer ward with shared rooms and an outpatient cancer treatment center with open space caused a significant TB spread among 1/4 of exposed pediatric cancer patients.
- Korean pediatric cancer patients' parents have a high rate of LTBI but they are not evaluated for LTBI despite spending a significant amount of time in the cancer ward and outpatient clinic with their children.
- Further policy is needed to prevent the TB outbreak caused by the parents in a pediatric cancer ward.