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Utility of the Teleconsultations in the Pulmonary Pathology Cases

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The request for the outside consultation is a practised procedure in pathology especially in a narrow subspecialization. Telepathology (TP) has become more relevant method for the daily routine in pathology. The study was performed to estimate the efficiency and the diagnostic accuracy of the static TP [sTP] in the consultations of some controversial pulmonary pathology cases as well as to demonstrate our experiences in sTP service. Thirteen controversial cases of the thoracic pathology were sent for the teleconsultations. The diagnosis made by referring pathologist [ref-Path] and captured microscopic images (selected from histologic slides) were prepared at QPD (Warsaw) using the "SAMBA 2005" system with "Telepath" software. The number of images/cases ranged from 10-38, exceptionally 49 and 85. The image files (1.8-10.5 MB) together with the patients' clinical data and HRCT photographs were transmitted via Internet, to the telepathologist [TPath] in the Thoraxklinik (Heidelberg), in the AFIP (Washington DC), or in the CLS (Calgary). For the quality assurance the same glass slides of 6 oncological cases were reviewed by TPath [rev-TPath] with a conventional microscope. The diagnostic problems presented by the ref-Path referred to 7 pulmonary oncology cases and 6 cases of interstitial lung disease. Some rare entities were included in the consulted cases, such as pulmonary plasma cell granuloma, metastatic uterine benign leiomyoma, neuroendocrine carcinomas, primary small cell carcinoma of pleurae, mediastinal B-cell n-Hodgkin's lymphoma of the diffuse large cell type, alveolar proteinosis related to a bacterial infection. The e-mail process was successful in all cases, the answers were faxed in 24-72hrs. The diagnoses of 6 oncological cases were concordant for the important diagnoses prepared by ref-Path, TPath and rev-TPath. The proper selection of the microscopic fields by ref-TPath as well as the experience of TPath helped to solve the diagnostic problems or improved the quality of diagnoses. The implementation of sTP remarkably shortened the time of consultation and allowed for early therapy. Our study proved the efficiency and high diagnostic accuracy of sTP for diagnostic consultations in the thoracic or pulmonary pathology problems.

KEY WORDS: *Static telepathology; Pulmonary pathology; Diagnostic teleconsultation*

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INTRODUCTION

Telepathology [TP] has become more relevant method for the daily routine in pathology all over the world but it is not so common in Poland [3, 6, 10, 14, 18]. Although several Polish Academic Centres have lately been equipped with TP systems and have introduced this method locally, TP has not been developed widely enough to be used in routine domestic service [16]. Slow development of telecommunication network, uncoordinated quality control system in pathology, in association with some economic problems, have interfered with the progress of telepathology activities in our country.

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The Institute of Tuberculosis and Lung Diseases [ITB&LD] in Warsaw is the referral centre for lung cancer therapy and the consultation centre for interstitial lung diseases in Poland. The static-imaging telepathology [sTP] has recently been implemented at DQP of ITB&LD for the diagnostic international consultations in the pulmonary and thoracic pathology problems. The spectrum of diagnostic problems occurring in the pulmonary pathology , similarly to other pathology subspecializations, comprises either rare entities or common diseases with unusual clinical-pathological presentation, as well as the problems related to the quality of examined material (small or traumatized samples).

AIMS

The study was performed to:
- explore the efficiency and diagnostic accuracy of sTP used for diagnostic consultations in the controversial thoracic oncology cases and interstitial lung diseases,

- evaluate the consulted interesting material and our experience in sTP service

MATERIALS AND METHODS

Thirteen histopathological cases, which had been consulted at DOP (May 2000 - Feb. 2001) entered the study: group A - 7 oncological cases (1A-7A); group B - 6 cases of the interstitial lung diseases (1B-6B). The detailed statement of studied cases is presented in Tables 1 and 2. Twelve patients (pts) were cured at ITB&LD.

Table 1. The clinico-pathological characteristic of the cases belonged to the group A

No	Patients: sex, age (ys)	Biopsy material	Spectrum of histopathological diagnosis	Ref-Path diagnosis / diagnostic problem
1A	F, 54	*bronchial wall (bronchoscopy)	* metaplastic squamous epithelium with dysplasia	* invasive squamous carcinoma
2A	M, 54	*nasopharynx *sinusal mucosa	*Wegener's granulomatosis	* B-cell n-Hodgkin lymphoma of diffuse large cell type
		*skin		* B-cell n-Hodgkin lymphoma of diffuse large cell type
3A	M, 66	* mediastinal pleura (radiograms suggestive of mesothelioma)	* pleural n-small cell ca with NE differentiation (Syn +, Chrom.A +)	* pleural n-small cell ca with NE differentiation ? *Problem*: unusual cytology
4A	M, 48	*bilobectomia 2 tumours		*1-combined NE ca ? *2- squamous ca with NE differ. *Problem*: two synchronous tumours or meta of tumour 2 to 1
5A	F, 66	* bronchial wall * cytological aspirate (bronchoscopy – 2x) * resected colon with adenocarcinoma	* proliferating bronchial epithelium, necrotic masses. No carcinomatous foci.	* tiny foci of adenocarcinoma necrotic masses (scanty material) *Problem*: metastatic colonic adenoca or primary adenoca of lung?
6A	F, 54	* lung biopsy (recurrent hemoptysis; hysterectomy done 10ys ago - benign leiomyoma)		*Problem*: interpretation of the microfoci of proliferating smooth muscles and microvessels - in lung parenchyma
7A	M, 26	* lung and pleura * lung parenchyma	* n-specific chronic interstitial inflammation * MALTOMA	* plasma cell granuloma, LIP (lymphoid reactive interstitial infiltrates).

Legend: NE - neuroendocrine

Table 2. The clinico-histopathological characteristic of the cases belonged to the group B

No	Patients: sex, age (ys)	Biopsy material	Spectrum of histopathological diagnoses	ref- Path diagnosis/ diagnostic problem
1B	F, 70	* lung biopsy	*BOOP	*alveolar proteinosis, organising pneumonia
2B	M, 36	* lung biopsy	*interstitial fibrosis	Interstitial inflammation with lymphocytic infiltrates, rich histiocytic component, mild fibrosis.
3B	M, 52	* lung biopsy * mediast. LN		Pt's profession: welder *chronic n-specific interstitial inflammation, end stage * burnt out histiocytosis X (CD1a neg)?
4B	F, 12	* lung biopsy	*Wegener's granulomatosis, lymphomatoid granulomatosis, bronchocentric granulomatosis	*Wegener's granulomatosis
5B	F, 42	* lung biopsy	*purulent bronchitis, bronchectases, interstitial inflammation	*bronchocentric destructive inflammatory process related to fungal infection (negative Grocott's staining).
6B	F, 50	* bronchial wall (bronchoscopy) * mediast. LN	*clinical problem: unknown cause of hemoptysis and bronchial haemorrhage. *inflammation, granulation *granulomatous lymphadenitis	*inflammation with necrosis, vascular malformation ? *granulomatous lymphadenitis

An unusual clinical course of either uncommon pathological presentation of the diseases, or because of discordance in the pathologists' opinions required a consultation with other experts in pulmonary pathology. In 5 cases (1A, 2A, 7A and 1B, 2B), the diagnosis of the referring pathologist [dgn-ref-Path] differed in the main statement, from the previously prepared pathological reports. In 5 cases, the referring pathologist [ref-Path] had a conceptual problems with the interpretation of the morphological lesions occurred in the cases: 4A, 6A, 2B, 3B and 6B (Tables 1 and 2). The probable (uncertain) dgn-ref-Path, resulted from the scanty material (as in case 5A) or negative special staining (Grocott's met.) for a pathogen (fungal?) infection (as in case 5B), required a diagnostic support from the expert TPath.

The sTP was implemented for the teleconsultations with the Thoraxklinik (Heidelberg), with the CLS (Calgary), or with the Armed Forces Institute of Pathology [AFIP] (Washington D.C.). Two TP centres had a telepathologist [TPath] in solo practice, while in AFIP there was a group of pathologists - experts in pulmonary pathology, gastro-intestinal pathology and cytopathology. A single referring pathologist from DQP presented a diagnosis or diagnostic problem to TPath. The diagnoses of TPath [dgn-TPath] were faxed in 24-72 hrs to DQP. For purpose of quality assurance the glass slides of 6 oncological cases were mailed or personally presented to the TPath for re-examination with a light microscope, to form the verified diagnosis [dgn-ver-TPath].

Static Image Capture. The static image files were prepared at DQP, using the computerised image analysis system "SAMBA 2005" with software for telepathology (Inc. Unilog, France). The system "SAMBA 2005" incorporates a microscope OLYMPUS BX50, the colour camera 3CCD (Sony), PC Pentium 133 MHz computer running under Windows 95. The digital video camera was operated at 768 x 576 pixels; the standardised JPEG image compression algorithm was used.

The microscopic fields chosen for transmission and the number of static images per case were at the discretion of the ref-Path and depended on the diagnostic problem. The microscopic static images were captured at 10x4x, 10x10x, 10x20x and 10x40x magnification. In the group A - the number of images per case ranged from 14 to 31 (median - 22); in the group B - ranged from 20 to 38 (median 28) except for 2 exceptionally huge files composed of 49 images (case 3B) and 85 images (case 2B). The volume of image-files ranged from 1.8 to 7.2 MB - in the group A; and between 5 to 10.5 MB in the group B. The dgn-ref-Path was transmitted via Internet along with the static-image files, with the clinical data and with CT scans of the patients (cases: 7A and 3B).

RESULTS

The first image-files transmissions failed due to unconventional software of the ITB&LD server and an indirect transmission was implemented via the server of the Warsaw Polytechnic. When the modified software on our sever was used, no procedural errors occurred in the e-mail process of the following cases.

Table 3. The group A: the detailed statement of the diagnoses prepared by TPath and rev-TPath, in comparison to dgn-ref-Path.

N	Case	Ref-Path diagnosis / diagnostic problem	TPath diagnosis	Rev-TPath diagnosis
1	1A	invasive squamous ca	invasive squamous ca	invasive squamous ca
2	7A	plasma cell granuloma, LIP	plasma cell granuloma, LIP	plasma cell granuloma, LIP (preleukemia)
3	3A	n-small cell ca with NE differentiation of pleurae (Syn +, Chrom.A +)? *Problem*: unusual cytology ?	small cell ca of pleurae (composed of larger cells)	small cell ca of pleurae (composed of larger cells)
4	6A	*Problem*: interpretation of the microfoci of proliferating smooth muscles and microvessels in lung parenchyma?	Early metastatic foci of benign uterine leiomyoma Proposed ihc: estrogen and progesteron receptors (for hormonal therapy)	Early metastatic foci of benign uterine leiomyoma
5	4A	*1-combined NE ca ? *2- squamous ca with NE differ. *Problem*: two synchronous tumours or meta of tumour 2 to 1?	*1-combined NE ca ? *2-squamous ca with NE differ. Problem can not be solved univocally without previous history.	*1-combined NE ca ? *2- squamous ca with NE differ. Problem can not be solved univocally without previous history.
6	5A	tiny foci of adenocarcinoma necrotic masses (scanty material). Dgn: probably metastatic colonic adenoca.	tiny foci of adenocarcinoma necrotic masses (scanty material). Dgn: probably metastatic colonic adenoca. Paraffin blocks requested for ihc.	tiny foci of adenocarcinoma: necrotic masses (scanty material) ihc in resected colonic adenoca: CK7+, CK20-, TTF1-. Ihc in brochoscopic material – inconclusive Dgn: probably metastatic colonic adenoca
7	2A	B-cell n-Hodgkin lymphoma of diffuse large cell type	B-cell n-Hodgkin lymphoma of diffuse large cell type (additional ihc requested)	

Legend: ihc – immunohistochemical staining

The results of teleconsultations are summarised in Table 3 and 4. The TPaths confirmed the diagnoses of the ref-Path in 5 out of 7 oncological cases (group A); in 2 cases TPath solved the conceptual diagnostic problems (cases 3 A and 6A). The cytology of the primary carcinoma spreading along the pleura, according to the TPath opinion, fits better to small cell carcinoma composed of larger cells (case 3A). From the experience of the TPath, small cell carcinoma growing in the pleura is usually formed by larger cells (spoken information by Prof. K. Kayser). In case 6A the parechymal microfoci of the proliferating atypical smooth muscles and microvessels were characteristic for early metastasis of the benign uterine leiomyoma. The immunohistochemical staining for estrogen and progesterone receptors were advised by the TPath for further hormonal therapy.

There was a complete concordance in the dgn-TPath and dgn-rev-TPath in all of 6 oncological cases.

There was an agreement in the ref-Path diagnosis and the TPath diagnosis for 5 out of 6 cases representing diagnostic problems of the interstitial lung diseases (cases 1B, 3B, 4B, 5B and 6B).

Table 4. The group B; the detailed statement of the diagnoses obtained from the TPath and rev-TPath, in comparison to dgn-ref-Path.

N	Case	Ref-Path diagnosis / diagnostic problem	TPath diagnosis
1	1B	alveolar proteinosis, organising pneumonia	alveolar proteinosis, organising pneumonia
2	4B	Wegener's granulomatosis	Wegenere's granulomatosis
3	2B	Interstitial inflammation with lymphocytic infiltrates, rich histiocytic component Pt's profession: welder	BOOP related to external agents in terms of an extrinsic triggering/release of the disease.
4	3B	*chronic n-specific interstitial inflammation, end stage ? * burnt out histiocytosis X (CD1a neg.) ?	* chronic n-specific interstitial inflammation, end stage. Allergic eosinophilic process related to histiocytosis X but not real histiocytosis X.
5	5B	* bronchocentric destructive inflammatory process related to funal infection (negative Grocott's staining in 1slide only).	acute destructive necrotising bronchitis, which might be caused by fungus (favourite dgn but cannot be proved)
6	6B	* inflammation with necrosis, vascular malformation ? (very scanty sample)	* inflammation and necrosis: bronchectases? Bronchitis? Inconclusive dgn –very scanty sample.

The TPath contribution extended the differential diagnosis in the case 3B, by names of the closest entities probably related to the morphological process (allergic eosinophilic process related to histiocytosis but not real histiocytosis). In case 2B, the TPath found the relation between patient's occupational risk and the histopathological lesions in his lung (BOOP related to external agents in terms of an extrinsic triggering/release of the disease).

When the number of images and the volume of image-files were compared for both groups of diagnostic problems: oncology (group A) and interstitial lung diseases (group B), it appeared that a higher number of selected images was needed for a proper presentation of interstitial lung diseases diagnostic problems needs than for oncology cases. It is conditioned by more complex morphology of the interstitial lung diseases especially those of unusual or diffuse and nonspecific appearance.

DISCUSSION

Implementation of TP facilitates the communication between pathologists and benefits by the teleconsultations with expert pathologists. The static-image TP system, used in our study to provide consultations for difficult pulmonary pathology cases, highlighted the importance of TP for making a final and proper diagnosis. TP final diagnoses were important for the clinical decision in the presented cases. Very high concordance in the diagnosis of the ref-Path, TPath and rev-TPath was observed in the oncological cases as well as in the problems related to the interstitial lung diseases (dgn-ref-Path = dgn-TPath). The opinions of TPath not only supported ref-Path in some diagnoses, but also improved the quality of the diagnosis in a few controversial cases. In comparison to some previous traditional consultations of 2 months duration (case 7A), the implementation of sTP remarkably shortened the time of consultations to 72 hrs, in case with rev-TPath diagnosis to 3 weeks (maximum).

The morphologic diagnosis of tumour specimens with precise tumour typing remains the basis of almost all cancer treatments. The evaluation of different types of neuroendocrine lung tumours has a high biological, prognostic and therapeutic relevance. A

question of the histopathological differentiation between small cell and non-small cell carcinoma appears frequently in the routine work of pathologists. The background of this aspect is related not only to the pathologists experience but might result from the morphological heterogeneity of small cell carcinoma, what has been reflected by the histologic re-classifications of this neoplasm [4, 7, 17]. Small cell carcinoma is liable to be mistaken for large cell carcinoma if attention is concentrated on cell size and the presence of discernible amounts of cytoplasm. In cases of less common localisation of the small cell carcinoma (pleura, thymus) [1], the morphology of this carcinoma may confused the pathologist as it was noticed in our case 3A.

In the short discussion about diagnostic problems regarding neuroendocrine tumours the case 4A should be mentioned. From the clinical point of view, the presence of two separate tumours in one lung lobe was not very unusual; however, the morphological components of both tumours created unsolved generic problem. Multiple lung cancers with neuroendocrine features are extremely rare and only one case was reported in the literature [12]. The presence of two tumours in one lung lobe of our patient arises two questions: is it synchronous double primary lung cancer with neuroendocrine features? Or is it one primary tumour with its metastasis? A certain answer could not be given to any of the questions aroused by the ref-Path, without knowing a previous history of the patient (which was unavailable in this case).

The group of rare entities is extended by: pulmonary plasma cell granuloma (s. inflammatory pseudotumour, s. inflammatory myofibroblastic tumour) - case 7A and metastasising benign uterine leiomyoma to the lung - case 6A. Plasma cell granuloma is a relatively discrete nonneoplastic mass and originates as an organising pneumonia in most cases. The histologic appearance depends upon the type and relative number of inflammatory and mesenchymal cells [2, 9]. Unusual clinical presentation of this tumour, associated with a diffuse interstitial infiltrates of the plasma cells and lymphocytes in both lungs, was the cause of some controversy among pathologists.

Random publications of the metastasising uterine benign leiomyoma refer to the well developed metastatic nodules in the lung [8, 13], which have very characteristic morphology and are recognised by the pathologists without any difficulties. In our case, we dealt with a very early stage of metastases appearing as microfoci of the proliferating atypical smooth muscles in association with microvessels. The dgn-TPath was very helpful in the proper interpretation of the pulmonary lesions in our patient.

Interstitial lung diseases include a broad spectrum of the diseases with more or less accurate histologic diagnostic criteria. Some entities are easy to be recognised for the experienced pathologist, when a representative material is available. Our cases: 1B - alveolar proteinosis with organising pneumonia, and 4B - Wegener's granulomatosis can be placed into this category. The teleconsultations for those cases were arranged because of a significant discordance between the dgn-ref-Path and previous histopathologic reports. There was a complete agreement between the dgn-ref-Path and the dgn-TPath

Specific diagnosis is considerably less frequent in diffuse lung diseases than in localised lesions, particularly in chronic diffuse lung diseases when nonspecific findings are common. The histologic slides of the lung biopsy of the case 3B showed the diffuse and advanced nonspecific interstitial inflammation (the end stage) which did not fit to any of well recognised entity. A descriptive diagnosis of the ref-Path emphasised that the lesions were difficult to be classified. The same category of the diagnostic problem faced the TPath, who confirmed the dgn-ref-Path and named the clinicopathological entities to which it came closest (allergic eosinophilic process related to histiocytosis).

In acute lung diseases, the diagnosis of infections are quite common. The fungal infections are mainly characterised by a necrotising granulomatous inflammation (with a variable amount of acute inflammation and eosinophilic component). The fungal hyphae identified in the background tissue is crucial for the diagnosis. The negative results of the microbiological and morphological (special staining) examinations could not prove the presence of the fungal pathogen in the case 5B, although the ref-Path impression as well as TPath favourite diagnosis were around such opinion. Unsuccessful treatment of patients against a broad spectrum of pathogens leads the clinicians to a choice of anti-fungal therapy. The remission of the lung lesions (proved by the radiological examination) confirmed indirectly the fungal infection as a cause of the pulmonary inflammatory process, in this case.

Referring to the case 2B, siderosis is the most frequent among the "benign" pneumoconiosis, and is caused by occupational exposure to iron occurring during iron mining, iron refining or various stages in steel manufacturing (e.g. welding). Siderosis is a radiological disorder and in the form of pure siderosis is not associated with respiratory symptoms of functional impairment. The symptoms of interstitial fibrosis, which is sometimes found in welders (welder's pneumoconiosis) is simply a siderosis with coexisting silicosis [11, 15]. The BOOP pattern morphology seen on the background of mild interstitial inflammation and fibrosis in the lung of the young welder (case 2B) was interpreted by TPath, as BOOP condition triggered/released by the external to the airways agents (related to the patient's profession). BOOP is increasingly recognised in association with a variety of systemic illness, immunological disorders, infections and exposure to toxic fumes or triggered by other external agents [5].

Tissue obtained by bronchoscopic biopsy is usually small and because of the size of the biopsy, there is always inherent sam-

pling error or a possibility of misinterpretation. Diagnostic categories of tissue from bronchoscopic biopsy are: specific histologic features (e.g. tumour or infections), characteristic changes (e.g. sarcoid) and entirely non-specific findings (e.g. inflammation in the bronchial wall). In our material presented to the teleconsultation were 3 diagnostic problems related to the bronchoscopic biopsy: the cases 1A, 5A and 6B. Unknown cause of the recurrent hemoptysis and the bronchial haemorrhage, in the history of 50ys women put the clinical attention to the bronchial tree lesions. However the results of radiological and bronchoscopic examination were inconclusive. Very tiny bronchial biopsy showed only a piece of granulation with necrosis. The histology of the mildly enlarged mediastinal lymph nodes, showed granulomatous lymphadenitis. The requested teleconsultation couldn't solve the clinical problem, but the dgn-TPath supported the ref-Path opinion.

The necessity for teleconsultations, in case 1A and 5A, was associated with the significant discordance between the ref-Path diagnosis and the previous opinions of the pathologists . Both cases belonged to the oncological pathology and represent quite common diagnostic problem for the pathologists. Small bronchoscopic biopsy with severe inflammation/ulceration in the bronchial wall or with necrotic masses, in a background of the neoplastic growth caused difficulties in the proper evaluation of such samples. Additional problem of the case 5A concerns the differentiation between metastases of the colonic adenocarcinoma and primary pulmonary adenocarcinoma. Usually, the utility of the special techniques like immunohistochemistry or electron microscopy can increase the probability of the accurate diagnosis. The shortage of the diagnostic material (in the paraffin blocks) resulted in the probable final diagnosis of the group of experts TPath [AFIP], important for the patient therapy and supportive for the dgn-ref-Path.

CONCLUSION

The majority of the diagnostic problems of the pulmonary pathology were solved by the implementation of the sTP, proving the efficiency of this method in the pulmonary diagnostic teleconsultations. The high degree of concordance in the diagnoses of the referring pathologist, telepathologist and revised opinions of TPath, confirms the accuracy of sTP in experts teleconsultations of the thoracic oncology cases. The diagnostic problems related to the interstitial lung diseases especially those of non specified entities have the same degree of difficulties in teleconsultations as those problems occurring in the conventional microscopy examination. Because of their complex morphology, the interstitial lung diseases need to be presented by a higher number of images (than oncological problem) to give a representative opinion for the telepathologist. The proper selection of the microscopic fields for static-imaging TP is a crucial factor in the diagnostic teleconsultations and allows avoid discordance in the diagnosis. The review of the consulted cases highlights an educational role of TP in getting experience in pathology as well as in service of TP system.

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